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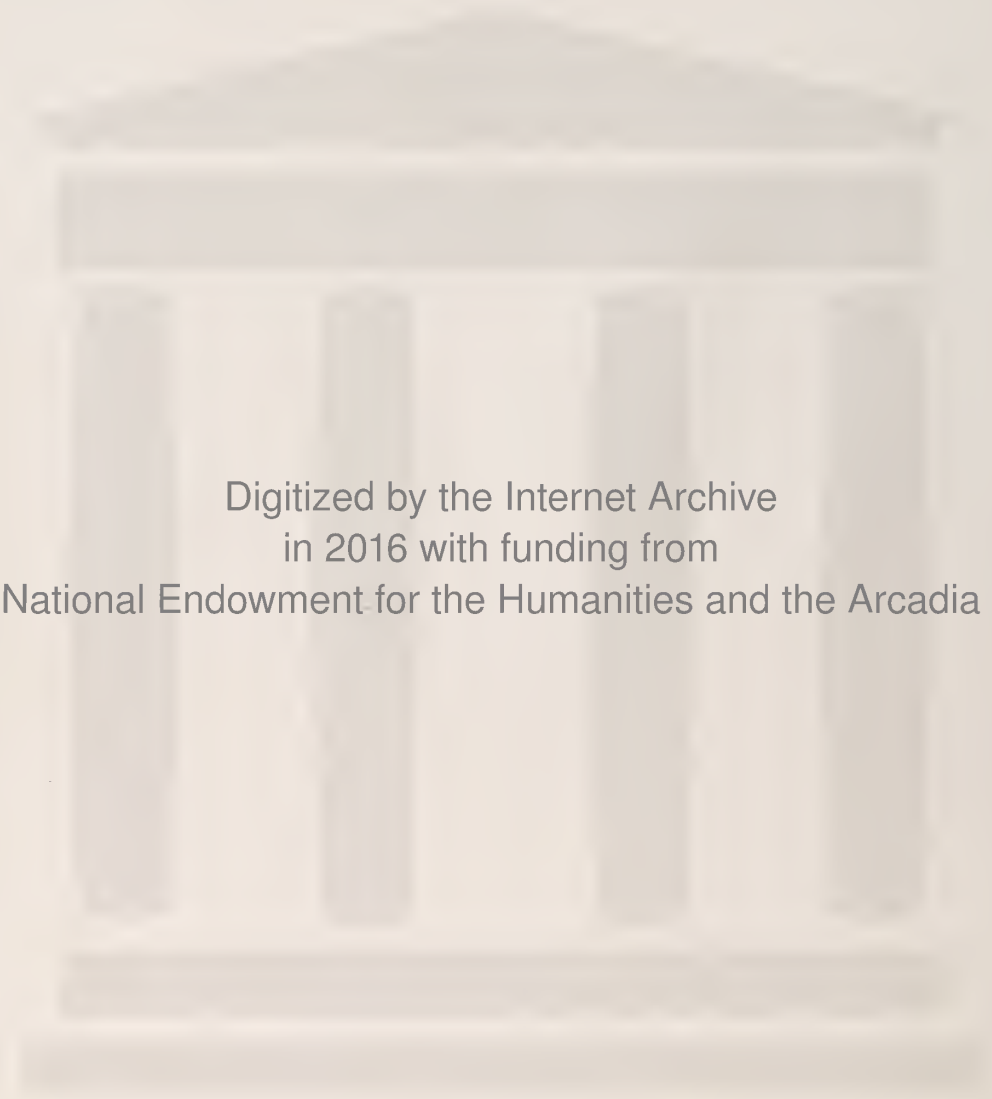


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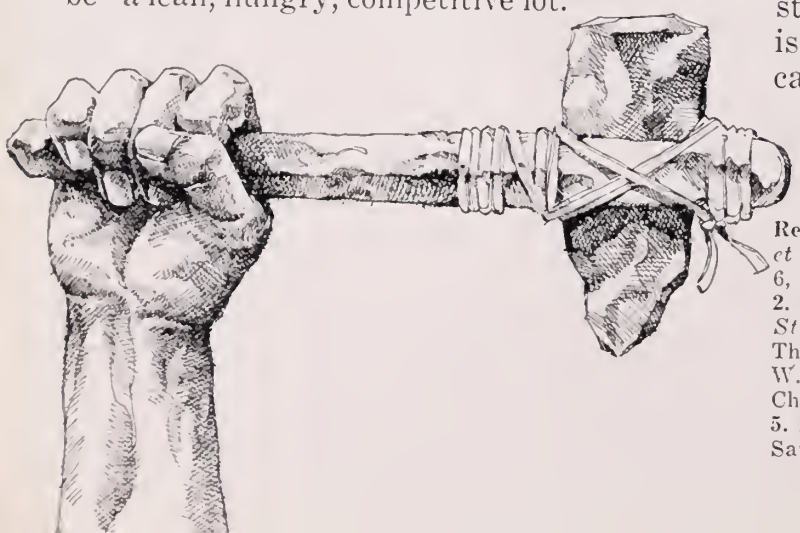
IF MORE MEN CRIED



At least seventy-five out of one hundred adults with duodenal ulcers are men.[1] Why? It may be significant that duodenal ulcer patients tend to crave recognition and are "especially vulnerable to threats to their manly assertive independence."[2]

Hypersecretion—an atavistic response. Stewart Wolf, who, with Harold G. Wolff, studied the personalities of duodenal ulcer patients, wonders if masculine competitiveness is related to "an atavistic urge to devour an adversary." It is striking, he reports, that an accentuation of gastric acid secretion and motility can be "induced in ulcer patients by discussions that arouse feelings of inadequacy, frustration and resentment."[2]

By chance? A lean, hungry lot. Was the link between emotions and gastric hyperacidity acquired through mutation to serve a purpose? During man's jungle period of evolution, the investigator points out, a male dealt with a foe by killing and devouring it. "It may be more than coincidence," he concludes, that peptic ulcer patients appear to be "a lean, hungry, competitive lot."[3]



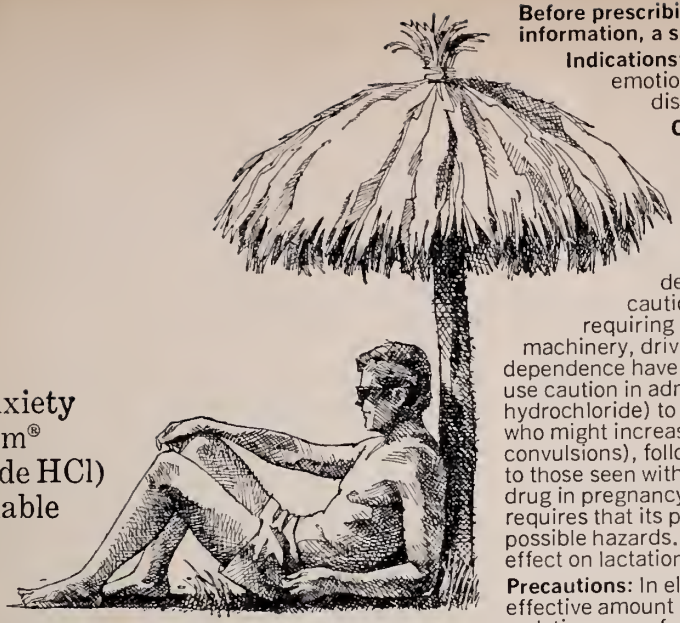
Big boys don't cry. If more men crie maybe fewer would wind up with duoden ulcers. But men will be men—the sum total their genes and what the are taught. Schottstaed observes that when mother admonishes he son who has hurt himse that big boys don't cry, sh is teaching hi stoicism.[4] Crying is th negation of everythin society thinks of as manly A boy starts defending hi manhood at an early age



Take away stress you can take away symptoms. There is no question that stress plays a role in the etiology of duodenal ulcer. Alvarez[5] observes that many a man with ar ulcer loses his symptoms the day he shuts up the office and starts out on a vacation. The problem is, the type of man likely to have an ulcer is the type least likely to take long vacations or take it easy at work.

The rest cure vs. the two-way action of Librax. For most patients, the rest cure is as unrealistic as it is desirable. Still, the stress factor must be dealt with. And here is where the dual action of adjunctive Librax can help. Librax is the only drug that com-

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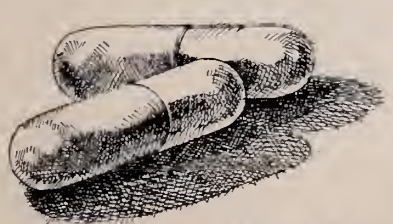


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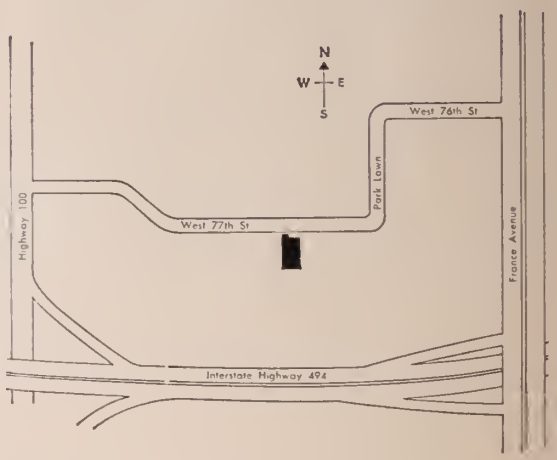
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President's Letter

Minnesota Pathologists

IN THE FACE of growing inefficiencies in all fields of human endeavor, the practices of anatomical and clinical pathology have struggled to become more accurate, efficient and up-to-date.

During the 1960s the pathologists developed quality control in the laboratories. This exercise alone greatly improved the proficiency and accuracy in the fields of clinical chemistry, blood banking, hematology, bacteriology and blood coagulation; and Minnesota pathologists were quick to incorporate these new ideas as well as to develop further methods for laboratory quality control.

During the latter part of the 1960s the large auto-analyzer of multiple chemical procedures became a common sight in Minnesota's larger hospitals, and soon clinicians recognized the value of a routine chemical profile on all hospital admissions. Numerous articles were written showing the discovery of unsuspected cases uncovered by the use of screening chemical procedures.

Soon smaller hospitals were developing their own profiles or sending them to larger laboratories. There was a feeling that one can't afford not to do a chemical profile since it often afforded speed of diagnosis on the first hospital admission. In the past, for instance, numerous hospital admissions were sometimes required in order to diagnose moderate hyperparathyroidism. The costs of these profiles were lowered in the face of climbing costs in the rest of the economy.

During 1970 many laboratories in Minnesota developed still further profiles, such as the anemia profile, lipid profile, kidney and liver profiles, in order to diagnose more rapidly and accurately. Chemical fingerprinting of the patient, or following the patient with an annual chemical profile started to become more popular and acceptable. In this way a change in the patient's BUN, for instance, shows up early. A BUN of 28 mgm% may not appear alarming in a 63-year-old patient. However, if it were 10 mgm% the year before and jumped to 28 mgm% in one year for no apparent reason, then further investigation seems necessary. Thus, 1970 appears to be the beginning of real preventive laboratory medicine.

In 1971 the Minnesota pathologists planned further work in quality control for all laboratories in the state with direction from the State Health Laboratories. Legislation is now in process in Minnesota in order to insure that laboratory quality control remains high in this state. Pathologists are also planning to offer better coverage to the smaller hospitals of the state with visitation from pathologists who will direct their laboratories, do autopsies and carry out frozen sections. We are planning better equipped regional laboratories functioning for the purpose of doing more complicated laboratory tests quickly and accurately for the physicians, smaller hospitals and patients of the state. As always we plan to make every effort to train good laboratory personnel and to keep in touch with the school systems of this state in order to inform the counselors of the different levels of laboratory workers.

It is through these efforts that the pathologists, with the help of their colleagues in this state, are hoping to prevent the weak from making the strong weak.

D. L. Michaelis, M.D.
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Valvular Competent Patent Foramen Ovale in Adults

RICHARD F. SCHROECKENSTEIN, B.S.*; GREGORY J. WASENDA† AND JESSE E. EDWARDS, M.D.

IN THE ATRIAL SEPTUM of the fetus, it is normal for a channel to be present through which vena caval blood (principally inferior caval) enters the left atrium.

A flap valve guards the channel called the foramen ovale: the so-called valve of the foramen ovale (Figures 1 and 2). At birth, with the onset

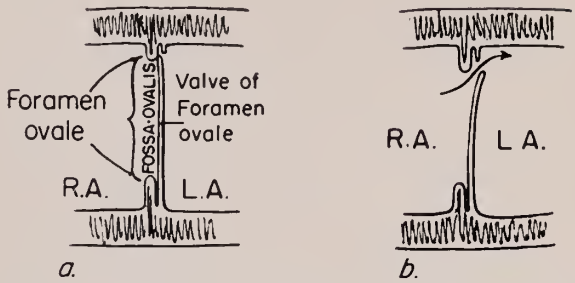


Fig. 1 Diagrammatic portrayal of the atrial septum at the region of the foramen ovale. R.A. = right atrial cavity; L.A. = left atrial cavity. The foramen ovale represents an opening in a component of the septum. On section it appears in two parts. Lying to the left of the foramen is a flap variously called the floor of the fossa ovalis or the valve of the foramen ovale. This flap responds to relative atrial pressures.

From the Departments of Pathology of the Charles T. Miller Hospital, St. Paul, Minnesota and the University of Minnesota, Minneapolis, Minnesota.

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*Medical Student Research Trainee.
†Research Assistant.

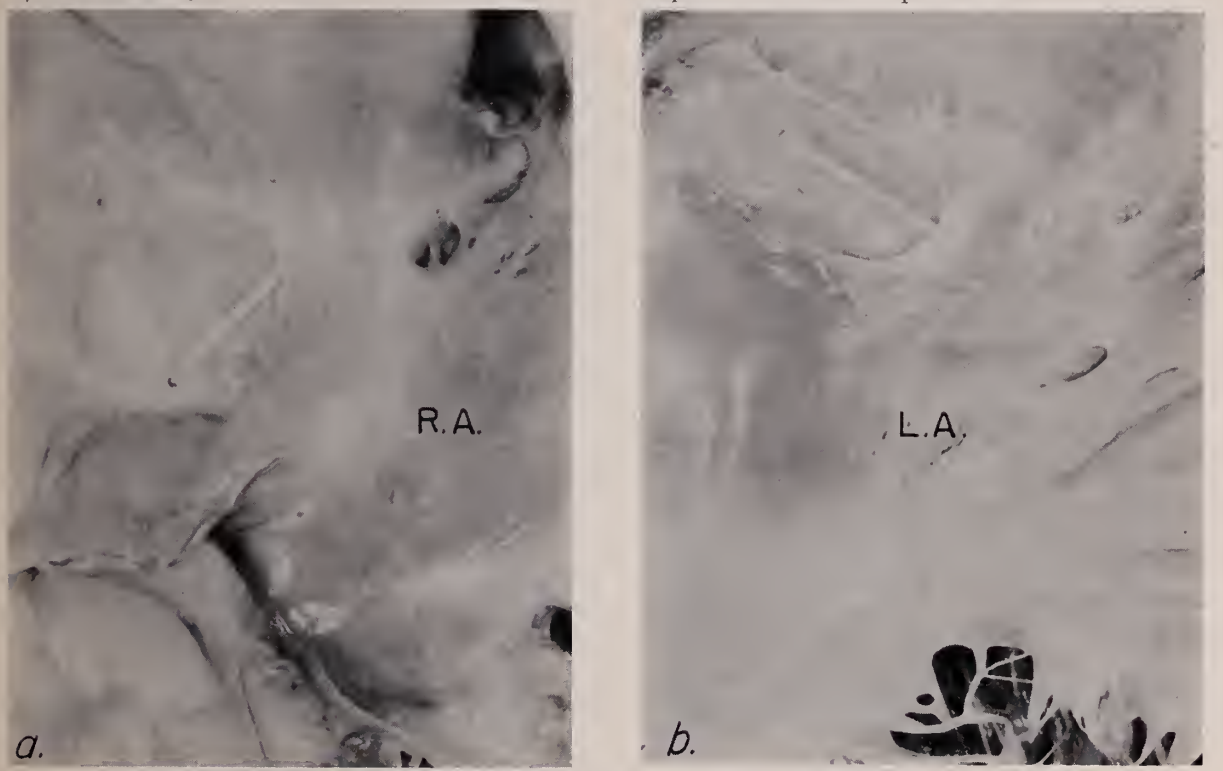


Fig. 2—Valvular competent patent foramen ovale in an adult. *a.* Right atrial (R.A.) aspect. The foramen ovale appears as a circle; the probe placed in the foramen disappears between the edge of the foramen and the floor of the fossa ovalis or valve of foramen. *b.* Left atrial (L.A.) aspect showing the probe placed in the foramen in *a* appearing in the left atrial cavity between the edge of the foramen ovale, on one hand, and the valve of the foramen ovale, on the other. The valve mechanism is such that left atrial pressure in excess of right atrial pressure would tend to close the potential opening.

of respiration, the associated increase in pulmonary blood flow results in a rise in left atrial pressure. This is turn causes the valve flap of the foramen ovale to close the foramen,[1] although episodes of right-to-left, transatrial shunting have been demonstrated in the first week of life.[1,2]

Later, there is a tendency for the valve of the foramen ovale to become adherent to the related structures of the atrial septum so as to cause permanent closure of the foramen ovale (Figure 3). In 1918 Scammon and Norris[3] found the foramen patent in 50 percent of subjects less than five years of age, while in individuals over the age of 20 years, the foramen ovale showed persistent patency in somewhat over 25 percent.

In 1938 Patten[4] reviewed the literature on the incidence of persistent patency of the foramen ovale in adults and found that, in general, this varied from 20 to 25 percent.

Patten named the condition of persistent patency of the foramen ovale, as it occurs in the normal fetus, *probe patent foramen ovale*. Later, one of us (JEE) and co-workers[5] introduced the term *valvular competent foramen ovale* for the same condition.

In view of the variations in incidence of valvular competent foramen ovale reported, we studied hearts obtained at necropsy at the Charles T. Miller Hospital from 144 subjects varying in age from the fourth through the ninth decades (30-89 years; the Table).

The majority of the subjects (112 cases) were in the sixth through the eighth decades, 60 percent of them male. In our material a variety of diseases was represented, including malignant tumors and various forms of cardiac disease principally of coronary and hypertensive types. Cases with congenital heart disease were not included.

There was no significant variation as to the nature of the foramen ovale in males as compared

TABLE

Years in Decades	Number of Cases
30-39	5
40-49	8
50-59	37
60-69	29
70-79	46
80-89	19
Total	144

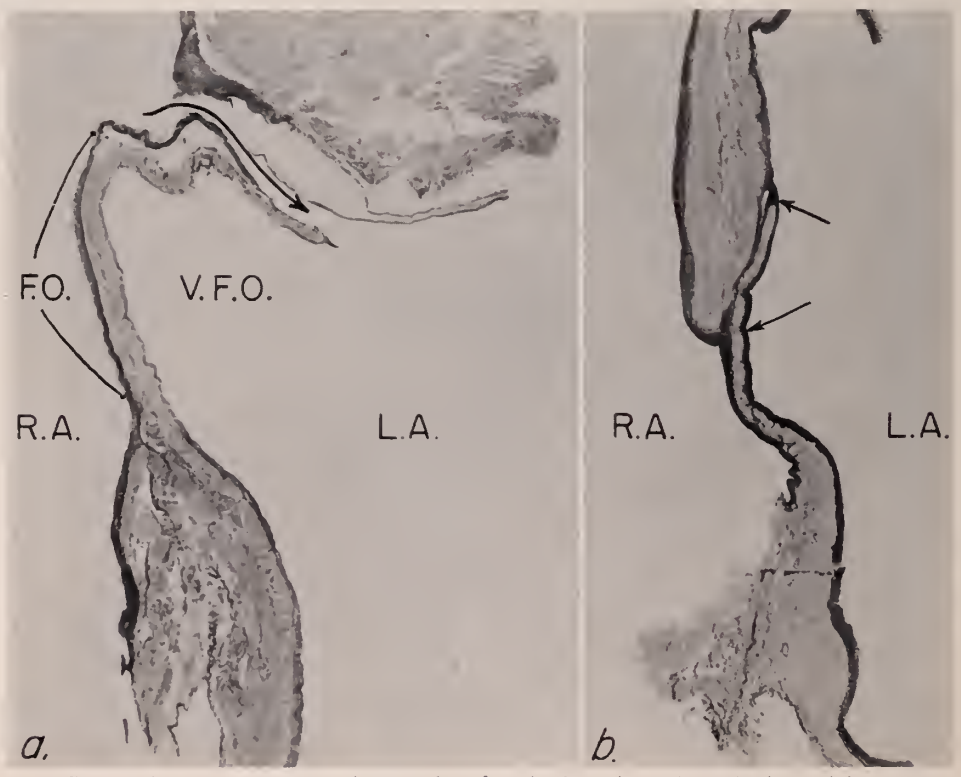


Fig. 3.—Low power photomicrographs of sagittal sections through the atrial septum in two cases. Perspective as in Fig. 1. *a*. The valve of the foramen ovale (V.F.O.) is not sealed to the foramen ovale, allowing a potential opening from right to left (arrow). *b*. The valve of the foramen ovale is sealed (arrows) to the atrial septum so that no potential opening is now present in this case.

with females among the various ages studied.

The average incidence of valvular competent patent foramen ovale in our material was 35.4 percent (Figure 4).

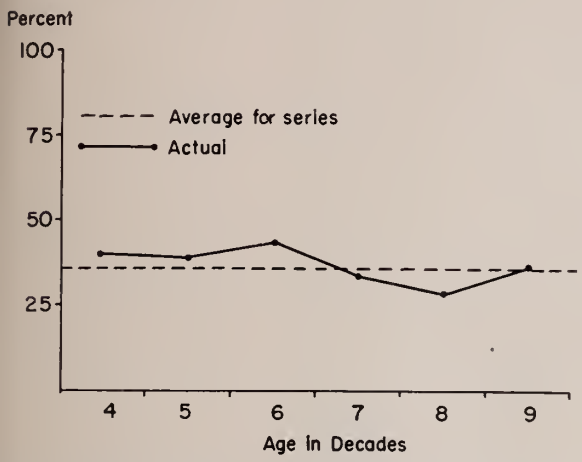


Fig. 4. Graphic portrayal of incidence of valvular competent patent foramen ovale in the various decades studied, the average being 35.4 percent.

Comment

This study on the incidence of valvular competent or so-called probe patent foramen ovale in adults revealed an average of 35.4 percent. This figure is higher than that generally quoted and may reflect the fact that, in this study, particular attention was directed to the foramen ovale. Reports using records of autopsies may yield a lower figure, as there is a tendency for a valvular competent foramen ovale to be overlooked unless a special point is made to determine the state of the foramen ovale.

Our study emphasizes that, in many adult subjects under proper circumstances, blood could potentially flow across the atrial septum.

When a valvular competent foramen ovale is present, its significance depends upon the relative pressures between the two atria. When a normal situation exists and the left atrial pressure is at a level only slightly above that in the right atrium, no flow occurs across the atrial septum. When the left atrial pressure rises to unusually high levels, as in mitral valvular disease, the valve may be pulled backward sufficiently as to create incompetence of the foramen ovale. The resulting left-to-right shunt may cause the right atrium and the foramen ovale to enlarge. The latter situation is a compounding one and may lead to a state in which a true atrial septal defect develops as a secondary condition.

On the contrary, when the pressure in the right atrium rises to a level above that in the left atrium and in the presence of a valvular competent foramen ovale, the valve of the foramen is pushed toward the left as a right-to-left shunt develops. Conditions which favor such an occurrence are right ventricular hypertension, as in pulmonary parenchymal disease, or the rare acquired pulmonary valvular stenosis. A common condition is recurrent pulmonary embolism. In this, once a right-to-left transatrial shunt has developed, further embolism may set the stage for paradoxical embolism.

Summary

Specimens of heart from 144 adult subjects were studied for the incidence of valvular competent foramen ovale ("probe patent foramen ovale"). This was found to average 35.4 percent, a figure higher than generally given in published accounts.

The results of the study emphasize that, in adult patients, a potential for transatrial flow of blood, especially a right-to-left shunt, is common.

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Historic Hospitals
The Bimaristan at Jundi Shapur



Anushirwan, Sassanian king and patron of the Bimaristan. Courtesy of the Smithsonian Institution, Freer Gallary of Art, Washington, D. C.

The primitive Christian civilization which followed the fall of the Roman Empire saw the emphasis in care of the sick pass to theological considerations and ideas of individual charity, to the neglect of Greek medical science. Greek medicine in this period was kept alive by a few scholars in the intellectual centers of Syria, but more prominently in the Persian Empire where a renaissance was building under the leadership of its Sassanian dynasty.

Most outstanding of the Sassanian kings was Anushirwan (531-579) who was a generous patron of the university at Jundi Shapur in southwest Persia, and of the hospital built opposite the university. The hospital was known as the Bimaristan, a Persian word meaning "place for the sick." Because of the great influence which this institution exerted over the Arab civilization in the centuries to come, the word "bimaristan" or simply "maristan" came to be the Arabic generic term for hospital.

At the Bimaristan Greek physicians mingled with Persian, Hindu, and Jewish scholars, synthesizing a new medicine, still modeled on Greek methods, but judged superior to all others. There was considerable stress on bedside teaching and on a free exchange of medical ideas. About 550 A.D. Anushirwan convened a symposium on medical subjects presided over by his own personal physician.

In 636 A.D. an Arab army invaded Persia and captured Jundi Shapur. The university and hospital were left undisturbed by the Arabs, but such was their admiration for these institutions that they gradually drained them of their leaders and trained staff to supply the similar hospitals which they built in their own cities.

There was a great interest in the therapeutic action of drugs at Jundi Shapur, and at the Bimaristan was published the first hospital pharmacopeia in history, a work of twenty-two volumes. The greatest Persian medical contribution of all, however, was the very concept of the medical hospital.

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Recurrent Pulmonary Embolism

From Upper Extremity Thrombophlebitis

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THROMBOPHLEBITIS of the upper extremity is usually considered a mild disorder, although associated pulmonary embolism has been reported.[1-3] The combination of *septic* thrombophlebitis of the upper extremity and pulmonary embolism is even more unusual and has been reported in severely debilitated patients with signs of lower extremity phlebitis as well.[1,4,5]

Like its counterpart in the legs, septic thrombophlebitis involving the arms is potentially hazardous. The present report illustrates the serious complication of septic pulmonary embolism and infarction following the development of septic thrombophlebitis from an indwelling polyethylene central venous pressure catheter in the arm. Absence of lower extremity thromboembolic disease was suggested on clinical grounds and confirmed by venography. Innominate vein ligation accomplished control of the disease.

Case Report

An otherwise healthy 46-year-old Caucasian male underwent uneventful right hemiglossectomy, hemimandibulectomy, and radical neck dissection with tracheostomy and tube esophagostomy for epidermoid carcinoma† of the tongue. Just prior to operation a polyethylene catheter was inserted percutaneously into the left median cubital vein and advanced into the right artium for central venous pressure measurement and fluid administration. The catheter was removed on the fourth postoperative day. There was no evidence of local infection or superficial phlebitis.

Infection

Eight hours later the patient's temperature rapidly rose to 39° C. even though administration of sodium cephalothin had been continued since the day of surgery. No source of infection was found. Treatment with chloramphenicol was begun empirically and the fever subsided.

The next day he again became febrile. Marked swelling, erythema, superficial venous distension, and tenderness extended from the medial aspect of the left arm into the axilla and over the upper anterior hemithorax. A firm, tender axillary cord was palpable. Continuous warm, moist soaks and a 10-day course of intravenous heparin were begun. In spite of repeated sterile blood cultures, chloramphenicol was continued, sodium cloxacillan was added and sodium cephalothin discontinued. The cellulitis had resolved by the tenth postoperative day.

He remained asymptomatic until the sixteenth postoperative day when fever and leucocytosis recurred. (These persisted during the next six weeks, the temperature ranging between 38-40° C and the white blood count between 15-20,000). No new source of infection was detected clinically. Although the chest x ray was clear, a heavy growth of *Pseudomonas aeruginosa* was cultured from tracheostomy aspirations. Since the initial febrile episode, cultures of tracheostomy aspirate for



Fig. 1—Chest film showing wedge-shapped density in the left lower lobe and associated pleural effusion consistent with pulmonary infarction.

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†Stage $T_3N_1M_0$.

Mycobacteria and fungi had been repeatedly negative.

Pulmonary Findings

On the nineteenth postoperative day, several small infiltrates appeared in the right upper and left lower lobes on chest xrays. Using ^{131}I-MAA (iodinated macroaggregated serum albumin), a lung scan showed areas of reduced perfusion at the right base. Intravenous heparin was reinstituted, and a five-day course of sodium colistimethate was started. Chloramphenicol and sodium cloxacillin were discontinued.

On the twenty-second postoperative day the patient noted hemoptysis and complained of left-sided pleuritic pain and dyspnea There was no clinical evidence of lower extremity thrombosis. Chest xrays showed a wedge-shaped density in the left lower lobe and a left pleural effusion (Figure 1). An electrocardiogram was normal. A left upper extremity venogram showed complete axillary and subclavian thrombosis with collateralization (Figure 2), while bilateral lower extremity venograms were normal. Subsequent serum lactic dehydrogenase and bilirubin values were compatible with a diagnosis of pulmonary embolism. Thoracentesis produced 200 ml. of bloody sterile fluid.

Additional infiltrates appeared serially, first in the right upper and then in the right-middle lobes, the latter containing an area of central rarefaction suggesting an abscess. The lung scan was repeated and was consistent with reduced perfusion of the entire right lung. Pulmonary angiograms showed multiple emboli in the middle and upper lobe branches of the right pulmonary artery. Repeated blood cultures remained sterile until the thirty-fifth postoperative day when *Staphylococcus epidermidis* was isolated.

Ligation of Vein

During the persistently febrile course, additional transient bilateral small pulmonary infiltrates appeared despite almost 50 days of heparinization, varied antibiotic therapy, and vigorous tracheal toilet. Accordingly, on the sixtieth postoperaitve day the left innominate vein was ligated through an upper median sternotomy. Bronchoscopic examination at operation was unremarkable. The patient's temperature promptly fell with concurrent clearing of the chest xray (Figure 3). Because of persistent copious tracheal secretions, his tracheostomy was reinserted two days later. All antibiotic therapy was discontinued 10 days following vein ligation. No new foci of pulmonary infection appeared. Although minimal edema of the arm occurred shortly after operation, there was no persistent edema, cyanosis or loss of function of the involved arm.

Comment

Septic pulmonary infarction is most often con-



Fig. 2—Venogram demonstrating occlusion of the axillary (arrows) and subclavian veins with extensive collateralization.



Fig. 3—(Left) Chest film before vein interruption showing right upper and lower lobe infiltrates and a left-sided pleural effusion secondary to multiple septic emboli. (Right) Film 10 days after vein interruption showing almost complete clearing.

fused with pneumonia or postoperative atelectasis. Chills, fever, pleuritic pain, hemoptysis and leukocytosis in various combinations are seen in all three conditions and are therefore not useful in the differential diagnosis. When adequate appropriate treatment for pneumonia or postoperative atelectasis is ineffective, the alternative diagnosis of septic pulmonary infarction should be strongly considered. As in our case, review of serial chest xrays will often reveal multiple patchy infiltrates which occasionally show areas of central rarefaction compatible with abscess formation.[8]

Venography is the best available method for confirming the diagnosis of thromboembolic disease and should be done promptly if the clinical impression is at all uncertain. After embolism had recurred in this patient, venograms of the left arm showed axillary and subclavian vein thrombosis. Although there was no clinical evidence of leg thrombosis, because of the rarity of embolism from the arm, venograms of the legs were performed. These were normal, substantiating the clinical impression that the septic emboli originated in the upper extremity. Indar[5] noted one instance of septic pulmonary infarction, presumably from the axillary vein, among the complications of indwelling polyethylene cannulae in the deep veins of 15 severely-burned patients. Crane[4] reported an instance of upper extremity septic phlebitis requiring venous interruption, and, although the patient had repeated pulmonary emboli, there was also associated saphenous phlebitis following bilateral lower extremity indwelling catheters. However, unless lower extremity throboembolic disease is excluded, the diagnosis of upper extremity thromboembolism remains highly suspect.[1] In our case the thromboembolic disease was clearly localized to the upper extremity.

The diagnosis of septic thrombophlebitis is often made on indirect evidence. In 93 cases, Neuhof[6] noted an inflammatory focus in 88%, chills in 66% and positive blood cultures in only 63%. Blood cultures were positive on only one occasion in this case. The growth of *Staphylococcus epidermidis* (albus), often regarded as a "skin contaminent," is seen frequently with intravenous catheter sepsis.[7] Unless treatment is adequate, one may anticipate extension of the process with development of acute bacterial endocarditis, septic pulmonary embolism and infarction, empyema, or metastatic abscess formation elsewhere.[5,8]

Initial management of septic thrombophlebitis includes an intensive course of intravenous heparin and antibiotics, extremity elevation, and local heat. Evidence of continucd sepsis, pulmonary consolidation or infarction are indications for *immediate* vein ligation proximal to the thrombus.[4,8] Although Neuhof in 1947 advocated excision of the infected vein,[6] more recent data[4] supports the conclusion that simple proximal vein ligation is sufficient when combined with intensive antibiotic therapy. Pyogenic foci elsewhere should be drained when present. Ligation and division of major upper exremity veins following thrombosis has not resulted in further edema or dysfunction of the extremity.[4,6]

Recent packaging of sterile catheters with large-bore needles for percutaneous insertion has made venous cannulation quite convenient and, by largely eliminating the surgical cutdown, has encouraged their use for *routine* administration of fluids. The most effective means of reducing venous thrombosis and sepsis from indwelling intravenous polyethylene catheters is to *restrict* their use to specific clinical situations—where a metal needle would be inadequate. The catheter should be removed as early as possible because: (1) a striking increase in positive catheter cultures and bacteremia occurs after 48 hours,[7,9] and (2) as in this instance, the absence of clinically apparent phlebitis may not reliably exclude deep venous disease and its hazardous potential.

Summary

A case of upper extremity septic thrombophlebitis giving rise to repeated septic pulmonary emboli was treated by proximal vein interruption. The disease followed the use of an indwelling venous catheter. Venography was valuable in the early diagnosis and specific localization of thromboembolic disease.

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See page 74 for balance of references.

Do Not Die

A "singing commercial" of penny-newspaper days tripped along like this:

Where'er Consumption's victims are,
In palaces or halls,
Or in the rural cottages,
With neatly white-washed walls,
Sink not into despondency,
There's naught for you to fear,
By the pale and flickering taper,
Or the brilliant chandelier;
But drink the draught, 'twil save you,
That bids Consumption fly,
Take DR. SWAYNE'S WILD CHERRY,
And do not, do not die!

Cherry pectorals were a flourishing item. They employed oil of almonds for the cherry flavor and a drug like morphine for the medical principle. Not all the blame falls on the package-medicine industry, however. Peddlers brought raw drugs to the back door. And many a regularly licensed doctor solved his diagnostic riddles with a dose of laudanum or paregoric.*

IT *LOOKS* LIKE WHISKY . . .
IT *TASTES* LIKE WHISKY . . .
IT *FEELS* LIKE WHISKY . . .
BECAUSE IT *IS* WHISKY!

Josh Billings, the popular cracker-box philosopher who panicked them in the 1870s and 1890s, said that if it was necessary to cheat in the "bitters" business, he hoped they'd cut down on the roots but not lower the base. Plantation Bitters, whose base was St. Croix rum, came in a brownish-amber bottle shaped like a log cabin, with a sloping roof. The nostrum first appeared during the Civil War when there was a heavy excise tax on whisky. The patents, being medicine, were exempt. The man behind the product was Colonel P. H. Drake, whose medication was promoted by means of a mysterious combination of letters and figures: "S. T. 1860 X." This bit of occult jargon appeared on fences, barns, billboards and rocks, on mountainsides and at Niagara Falls. It is said that Drake tried to paint his ad on Mount Ararat, the supposed landing place of Noah's Ark—see Genesis 8:4.

The explanation of "S. T. 1860 X" most commonly given was that the cryptogram meant: "Started trade in 1860 with ten dollars capital." But Drake insisted it didn't mean anything.

All the bitters boys put a generous amount of C2H50H into their formulas, "to preserve the medicine." To demonstrate how much, one enterprising doctor at the Battle Creek Sanitarium hooked up a can containing a tablespoon of Hostetter's Bitters to a gas burner and mantel. It had a "breath" that burned brightly for four full minutes. No wonder the medicine was often sold "on premises" by the drink rather than by the bottle, and that Colonel Hostetter made $18,000,000 out of his celebrated comforter.*

*Gerald Carson: One for a Man, Two for a Horse: a Pictorial History, Grave and Comic, of Patent Medicines.

OLD DOC HESS SAYS: Some people vote contrary to their conviction in order to demonstrate their broadmindedness.—C.O.R.

Polymyalgia Rheumatica with Temporal and Coronary Arteritis

A Case Report

NATHAN D. MOLLDREM, M.D.* and RONALD OLIN, M.D.†

PATIENTS WITH TEMPORAL (giant-cell) arteritis are known to have involvement of other medium and large-sized arteries. Polymyalgia rheumatica‡ is recognized as being related to giant-cell arteritis and may precede, accompany, or follow it.

The present report describes a woman with polymyalgia rheumatica who developed temporal arteritis followed one year later by probable coronary arteritis.

Case Report

A 65-year-old white housewife of Norwegian extraction was first seen at the Fargo Clinic on January 3, 1967, for evaluation of headaches of six weeks' duration. These were throbbing, generalized, and worse in both temples. Aspirin gave only partial relief. She also had pain in the jaw muscles with chewing and in the muscles of the gluteal areas and anterior thighs. The muscles of the shoulder girdle were not symptomatic. She denied any visual disturbance, fever, anorexia, or weight loss.

Past History

Over the preceding 15 years she had been treated elsewhere by several physicians for recurring myalgias and arthralgias. When 50 years old, she recalled pain in the low back and thighs associated with difficulty in walking. This was treated by weekly injections over a two-month period with some relief. When she was 52 years old, a tonsillectomy was performed because of these myalgias, and this helped for four to five years. When aged 62, she recalled difficulty with pain and stiffness of the neck and left shoulder muscles, and she again received a series of weekly injections with relief. Raynaud's phenomenon from exposure to cold and involving the index and middle fingers of both hands had been present for at least ten years.

Physical Findings

Physical examination revealed a thin, normally developed woman. She was 65 ¾ inches tall and weighed 128 pounds. Blood pressure was 152 systolic and 80 diastolic; pulse, 90 per minute, temperature, 99° F.; and respirations, 20 per minute. Funduscopic examination was normal. The temporal arteries were thickened and tender bilaterally (Figure 1). There was moderate tenderness to pressure of the gluteal and anterior thigh muscles. The arterial pulses were normal. The remainder of the physical examination was unremarkable.

Laboratory

Laboratory studies revealed a hemoglobin of 11.3 gm percent; hematocrit, 35%; and leukocyte count 7,350 per cmm with a differential of 30% lymphocytes, 1% monocytes, 59% segmented neutrophils, 9% band neutrophils, and 1% eosinophils. The erythrocyte sedimentation rate was 105 mm per hour (Westergren). The following labora-



Fig. 1—Shows thickened right temporal artery.

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‡See editorial page 47.

tory tests were normal or negative: routine urinalysis, VDRL flocculation test, latex fixation for rheumatoid factor, LE clot test, and serum transaminases. The serum cholesterol was slightly elevated at 291 mg percent. Chest x-ray was normal; x-ray of the cervical spine revealed minimal narrowing of the C-4 and 5 interspace and moderate narrowing of the C-5 and 6 interspace with surrounding lipping and spur formation; x-ray of the dorsal and lumbar spines revealed a minimal thoracic scoliosis and mild hypertrophic changes.

Biopsy of Artery

A biopsy specimen from the right temporal artery at the hairline revealed degenerative changes throughout all layers of the arterial wall with diffuse infiltration by chronic inflammatory cells, particularly in the outer layers of the media. There was marked subintimal fibrous proliferation and fragmentation of the internal elastic membrane. Giant cells were not numerous but were, nevertheless, present in the region of the elastic lamina and also throughout the media. The lumen was stellate and considerably reduced in diameter (Figure 2).

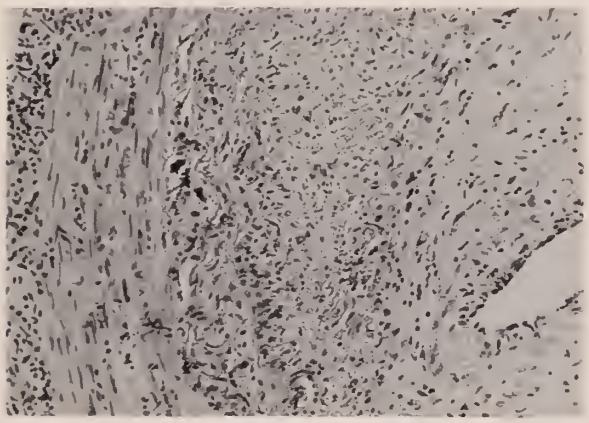


Fig. 2—Photomicrograph of right temporal artery showing diffuse infiltration by chronic inflammatory cells, particularly in the outer layers of the media, marked subintimal fibrous proliferation, fragmentation of internal elastic membrane, and giant cells in the region of the elastic lamina. Hematoxylin and eosin, X100.

Treatment and Progress

Following the biopsy she was started on prednisone, 60 mg daily. After one week the dosage was decreased by 5 mg. decrements at approximately 10- to -..-day intervals. When the daily dosage reached 30 mg, the decrements were changed to 2.5 mg at 10- to 14-day intervals.

The patient was reexamined on February 2, 1967, at which time she was taking 30 mg of prednisone daily. The headaches and pelvic girdle discomfort were no longer present and she felt well. The temporal arteries were no longer thickened or tender. The erythrocyte sedimentation rate was 16 mm per hour (Westergren). An incidental 12-lead electrocardiogram was normal. The prednisone dosage was then gradually decreased and discontinued on July 24, 1967.

In December 1967 the patient noted the gradual onset and worsening of pain and stiffness in the muscles of the neck, shoulders, upper arms, gluteal areas, and thighs, and for the first time a substernal "burning" pain radiating to the neck and coming on with moderate exertion. A 12-lead electrocardiogram now showed low T-waves in the standard leads and deep T-wave inversion in leads V-2 to V-6 (Figure 3). The sedimentation rate was 100 mm. per hour.

With the presumptive diagnosis of polymyalgia rheumatica and probable coronary arteritis, treatment was started with 60 mg of prednisone daily. She was also given nitroglycerin, 0.4 mg sublingually as necessary. When next seen on January 9, 1968, the shoulder and pelvic girdle pains were completely relieved and the effort angina was less frequent. A 12-lead electrocardiogram now showed higher T-waves in the standard leads and upright T-waves in the precordial leads (Figure 3). Prednisone was continued and slowly reduced at the rate of 2.5 mg every two to three weeks.

Comments

Hutchinson (1890) first described temporal arteritis in a man over 80 years of age who had "red streaks on his head," presumably the temporal arteries which later occluded, resulting in scalp necrosis. Horten et al. (1934) described two cases of temporal arteritis which they considered a focal localization of some unknown systemic disease resembling periateritis nodosa. Gilmour (1941) first used the term giant-cell arteritis. and Kilbourne and Wolff (1946) coined the term

TABLE I
Classic Temporal (Cranial) Arteritis

Incidence:	Over age 55 (46-88 years). Slightly commoner in women
Prodromata:	Malaise, weight loss, anorexia, slight fever, sweats, depression, myalgias
Clinic features:	Symptoms—Unilateral or bilateral headaches with pain and tenderness over the temporal artery; jaw pain on chewing; neck, occipital, and facial pain; diplopia and episodic amourosis fugax Signs—Reddened, thickened, nonpulsating temporal artery. Funduscopic examination showing retinal pallor, disk edema, and occasional hemorrhages
Laboratory findings:	Mild normochromic, normocytic anemia; normal or slightly elevated leukocyte count; erythrocyte sedimentation rate between 50 and 100 mm per hour; serum protein electrophoresis showing "stress pattern" of decreased albumin and elevated alpha-2 globulin
Biopsy:	Temporal artery showing a granulomatous infiltration primarily of the media and intima mith mononuclear and giant-cell infiltrations and lumen obliteration
Treatment:	Dramatic response to steroids which should be continued for six months; supplemental anticoagulants if blindness is imminant
Course:	Relapses common in usually less than two and a half years
Complications:	Irreversible blindness 5 to 25% of cases; scalp necrosis

cranial arteritis because of involvement of multiple branches of the common carotid artery. The classic picture of temporal (cranial) arteritis is outlined in Table 1.

Polymyalgia rheumatica was first described in detail by Swedish and European workers in the early 1950's. It received little attention in this country until Polanky et al. (1965) reported the first American case. The syndrome is briefly summarized in Table 2 and is considered one manifestation of a systemic giant-cell arteritis (Table 3). Neulengrecht and Schwartz (1952) described 78 patients with periarthrosis humeroscapularis with weight loss, fever and an elevated sedimentation rate. Barber (1957) first suggested the term polymalgia rheumatica in a report of 12 cases. Paulley (1956) was the first to suggest that the clinical picture of polymyalgia rheumatica was identical with the prodromic manifestations of temporal arteritis. This was confirmed by Alestig and Barr (1963) who demonstrated the characteristic giant-cell arteritis on biopsy of seven of 10 patients with polymyalgia rheumatica and asymptomatic, nontender temporal arteries. Hamrin, Jonson and Landberg (1964) verified this finding in 23 patients with polymyalgia rheumatica of

TABLE 2
Polymyalgia Rheumatica

Synonyms:	Senile arthritis. Arthritic rheumatoid arthritis. Pseudopolyarthrite rhizomelique. Periarthrosis humeroscapularis. Periextra-articular rheumatism. Myalgic syndrome of the aged with systemic reaction. Giant-cell arteritis of the aged
Incidence:	Estimated by Dixon (1966) to be similar to gout in the general population and half as common as rheumatoid arthritis at age 70. Age and sex the same as temporal arteritis
Prodromata:	Same as temporal arteritis
Clinical features:	Usually an insidious onset with prodromata and slow progression; occasionally an abrupt onset without prodromata; moderately severe shoulder and pelvic girdle pain and tenderness without weakness
Laboratory findings:	Same as temporal arteritis; blood studies of muscle enzymes and electromyography normal
Biopsy:	Muscles microscopically normal; temporal arteries showing giant-cell arteritis in over 50% of cases despite no headache or tenderness
Treatment:	Same as temporal arteritis
Course:	Usually benign and self-limited (six to eighteen months); occasionally protacted with relapses (two to five years)
Complications:	See Table 3

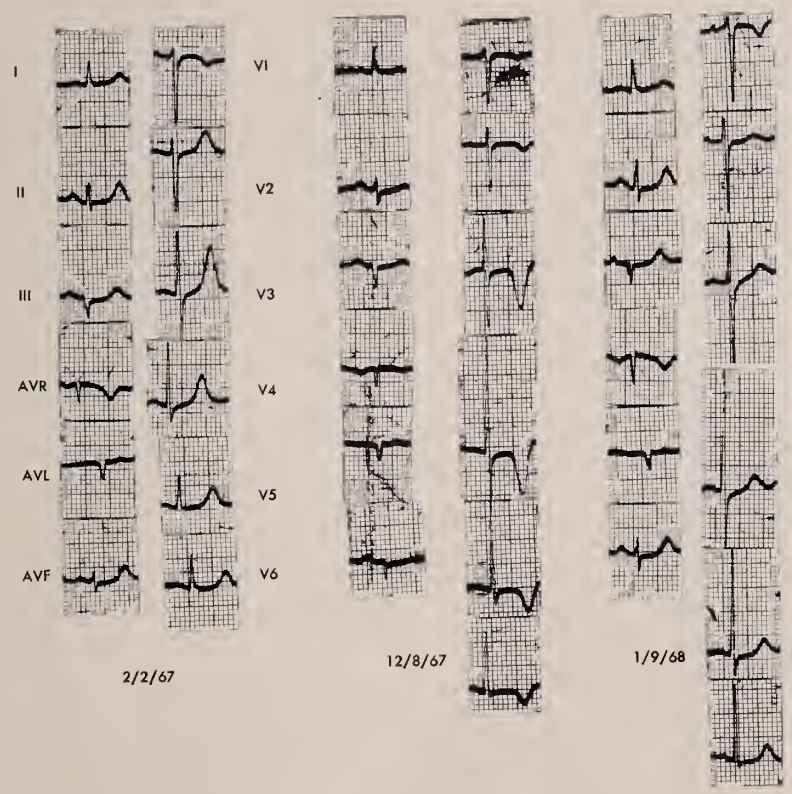


Fig. 3—Electrocardiogram tracings from three examinations.

which 21 had a biopsy of an asymptomatic temporal artery and 12 showed giant-cell arteritis and four nonspecific inflammation. This same group reported in 1965 that four of their patients demonstrated arterial stenosis on aortography of which four subsequently developed an aortic-arch syndrome. One patient came to autopsy which showed giant-cell arteritis of the involved vessels.

Paulley and Hughes (1960) in a classic study of 76 patients with giant-cell arteritis reviewed 15 case histories in detail and noted that 42 percent of patients presented with polymyalgia rheumatica and 39 percent with ocular manifestations. They outlined the protean manifestations of the condition and showed how these cut across all fields of medicine (Table 3).

TABLE 3
The Protean Manifestations of Giant-Cell Arteritis

Arteries	Clinical features	Selected references
Internal and external carotids and vertebrol-basilar and branches	Depression Psychosis Confusion Vertigo Deafness Blindness Cranial nerve palsies Hemiparesis Hemiplegia	Cordell and Hanley (1951) Crompton (1959) Fisher (1959) Paulley and Hughes (1960)
Aortic arch and branches (subclavian, innominate, axillary, and brachial)	Pulseless disease; variable combinations of occlusive or aneurysmal disease or both	Hunder and associates (1967)
Coronary	Insufficiency and infarction	Paulley and Hughes (1960) Morrison and Abitbol (1955)
Mesenteric, renal iliac, and uterine	Insufficiency and infarction syndromes	Russell (1959) Balmforth (1964) Cooke (1946)

Mortality

Mortality figures on giant-cell arteritis tend to vary according to the selection of patients. Schick (1958), in reporting 75 cases of temporal arteritis, noted no mortality. Mosher (1959) reported 11 deaths from vascular complications in 32 patients with giant-cell arteritis. Autopsy studies have shown involvement of the temporal, occipital, ophthalmic, carotid, vertebral, innominate, subclavian, aortic arch, mesenteric, renal, iliac, and uterine arteries. Crompton (1959) did a careful arterial dissection in a patient who died from a myocardial infarction with giant-cell arteritis in the coronary arteries and who presented with temporal arteritis and blindness. He demonstrated that the arterial involvement occurred in a skip rather than in a uniform distribution throughout the vessel. This would explain the tendency to aneurysm formation and the occasional negative biopsy of seemingly involved temporal arteries. This histologic picture was that of a panarteritis of medium and large vessels with giant-cell, granulomatous formation, fragmentation of the elastic fibers of the media, and intimal thickening producing obstruction of the lumen and thrombus formation.

A moot point is what actually produces the girdle-muscle pain in polymyalgia rheumatica. The muscles are normal histologically, by blood enzyme determination, and by electromyography, but the vessels supplying these muscles have never been examined in the acute phase of the disease. It is very likely that these vessels are inflamed, with the resultant ischemia producing the pain.

Differential Diagnosis

The differential diagnosis of giant-cell arteritis with polymyalgia rheumatica involves consideration of an occult malignancy, infection or lymphoma, rheumatoid arthritis, polymyositis, and periarteritis nodosa. Careful laboratory investigation and observation of cases over a prolonged period helps to rule out carcinoma, infection, or lymphoma. Rheumatoid arthritis is also ruled out by the absence of synovitis, joint destruction, and negative tests for rheumatoid factor. Polymyasitis causes girdle weakness with little pain and tenderness; muscle biopsy, blood enzyme studies, and electromyography are diagnostic. Periarteritis nodosa involves smaller arterioles and venules and has a different clinical spectrum and histologic appearance.

Our case presented with temporal arteritis and likely polymyalgia rheumatica involving the pelvic girdle muscles. We would be inclined to dismiss her previous 15-year history of intermittent myalgias and arthralgias as being due to fibrositis or muscular rheumatism rather than remissions and exacerbations of polymyalgia rheumatica. Despite the presence of headaches for six weeks, she did not experience any of the usual prodromata, which is unusual for temporal arteritis. She also had no visual disturbance or funduscopic changes, although intermittent claudication of the jaw muscles on chewing was present. The response to steroids was dramatic, and these were slowly reduced and discontinued in six months which, in

retrospect, was perhaps a little too early.

When seen again approximately one year after the onset of temporal arteritis, she demonstrated the classic clinical picture of polymyalgia rheumatica involving both the shoulder and pelvic girdles and angina with effort. The angina was likely on the basis of coronary arteritis rather than coronary atherosclerosis. Coronary arteritis has been described previously by Morrison and Abitbol (1955), Crompton (1959), and Paulley and Hughes (1960). Equal blood pressures in both arms and normal and equal pulses in the upper extremities seemed to rule out any significant degree of aortic-arch involvement, although minor involvement of the arch affecting the coronary ostia could not be ruled out without coronary angiography. The electrocardiogram had changed and showed ischemic changes. Again, the polymyalgia rheumatica and coronary arteritis responded dramatically to steroids. The electrocardiogram reverted to near normal after one month, which would be unlikely if the angina was caused by coronary atherosclerosis. Follow-ups revealed that she continued to do fairly well and steroids will be maintained for a longer period than for the previous episode.

Raynaud's phenomenon is unusual in giant-cell arteritis with polymyalgia rheumatica. The fact that it did not occur during the winters of 1967 and 1968 while she was taking steroids can probably be explained by the tendency of steroids to have a vasodilating effect.

The disease could continue to smolder for another one to three years before "burning out." It is conceivable, however, that the patient could develop other vascular manifestations of giant-cell arteritis in this interval.

Conclusion

Temporal arteritis and polymyalgia rheumatica should be suspected in any patient over 55 years of age who develops girdle muscle pains with or without involvement of medium and large-sized arteries anywhere in the body. The sedimentation rate may be elevated over 50 mm per hour and the response to steroid therapy can be dramatic.

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Laboratory Letter

So You Suspect Cushing's Syndrome

And well you might.

After all, Cushing's syndrome can present as diabetes, hypertension, obesity, osteoporosis, polycythemia, menstural problems, muscle weakness or wasting, hirsutism, mental disorders, purple striae, ecchymoses, or acne.[1] So many symptoms and signs might lead you to suspect Cushing's syndrome. But heretofore you have not had any simple and reliable means of excluding the diagnosis.

Urine tests for 17-ketogenic and 17-hydroxysteroids are reliable, but they are not simple. You have to instruct your patient how to collect a 24-hour urine sample; you may have to hospitalize him for accurate urine collection; and you have to worry about drug interference.[2] Besides, your patient, if he is saddled with the job of bottling his output at home, he has to stay next to a bulky container for hours; then suffer the indignity of carrying it around.

Serum Cortisol

If you wish to rule out Cushing's syndrome simply, you might consider ordering a serum cortisol. This test requires five ml. of serum, and but a few minutes of the patient's time for a venipuncture.

Proponents of the Single Dose Dexamethasone Suppression Test say you can screen for Cushing's with a single venipuncture for a serum cortisol determination.[3,4] You simply tell your patient to swallow a one mg. dexamethasone tablet between 11 P.M. and midnight. Then you instruct him to have his blood drawn for a serum cortisol test at 8 A.M. the next morning.

If the 8 A.M. value falls below 10 mcg./100 ml., you can essentially rule out Cushing's syndrome.[4] If the level exceeds 10 mcg./100 ml., you may have a case of Cushing's syndrome on your hands, and you should go ahead with definitive urine tests.

Clark T. Sawin, of the Boston Veterans' Hospital, believes a single test oversimplifies matters.[5] He suggests three venipunctures for serum cortisol levels—the first two at 8 A.M. and 5 P.M. to establish the patient's normal diurnal variation, and the third at 8 A.M. after one mg. of dexamethasone the previous night. According to Doctor Sawin, the normal range for the first 8 A.M. sample is 8 - 29 mcg./100 ml., for the 5 P.M. value 4 - 20 mcg./100 ml., and for the 8 A.M. value after dexamethasone less than 2.0 to 7.4 mcg./100 ml.

Reasoning

The reasoning behind the single and triple venipuncture methods is the same. Serum cortisol level of the normal person peaks at 8 A.M. (mean 16 mcg/100 ml.) and ebbs to its low point (mean) eight mcg./100 ml.) between 5 P.M. and 9 P.M. Dexamethasone taken between 11 P.M. and midnight suppresses the 8 A.M. value, usually below five mcg./100 ml. (mean four mcg./100 ml.).

Not so with Cushing's syndrome patients. Their plasma cortisols stay at high levels (usually above 20 mcg./100 ml.); don't fluctuate diurnally; and are not significantly suppressed by dexamethasone.

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Any pathologist wishing to contribute material for this section is invited to do so.

Neurofibromatosis and Hypertension

Due to Pheochromocytoma or Renal-Artery Stenosis

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THE OCCURRENCE of hypertension in patients with neurofibromatosis has been of interest over the years, particularly because of the relationship to pheochromocytoma. More recently, association of a number of vascular abnormalities with neurofibromatosis has been noted. Many of these patients are hypertensive, apparently because of neurofibromatous involvement of the renal arteries.

We reviewed the experience of the Mayo Clinic with combined neurofibromatosis and hypertension over a period of 20 years, and report here two of the cases with recent treatment. The hypertension was due to pheochromocytoma in one of these, and to bilateral renovascular stenosis in the other

Incidence

From 1950 through 1969, pheochromocytoma was diagnosed in 132 cases at this institution. The diagnosis was made preoperatively in 113 and confirmed by exploration. In the remaining 19, the discovery of the tumor was incidental to other surgery or autopsy. During the same period, neurofibromatosis was diagnosed clinically in approximately 600 patients, of whom 15 had sustained diastolic hypertension (greater than 90 mm. Hg.). The combination of pheochromocytoma and neurofibromatosis occurred in three cases—which amounted to 2.3% of the 132 with pheochromocytoma and 0.5% of the approximately 600 with neurofibromatosis. We had no cases of pheochromocytoma associated with Sturge-Weber syndrome, tuberous sclerosis, or von Hippel-Lindau syndrome. Excretory urography, carried out in the remaining hypertensive patients with





Fig. 1—(Case 1). Plexiform neurofibroma excised from posterior mediastinum. (Top) Multiple branching segments make up gross specimen. (Bottom) Fibrous appearance of abundant nerve elements. (Hemotoxylin and eosin; x 75.)

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neurofibromatosis, suggested the possibility of renal-artery disease in one case. Renal angiography was not done.

Case Reports

Case 1

An adopted white boy was first seen in 1952 at two years of age. Physical examination revealed café au lait spots and many neurofibromas. Blood pressure was 105/60.

At age five, the blood pressure was found to be 170/120 and funduscopic examination disclosed arteriolar narrowing, grade 1. Normal results were obtained from excretory urography and a phentolamine (Regitine) test for pheochromocytoma, and the plasma concentrations of catecholamines also were normal. A mass removed from the posterior mediastinum was identified as a plexiform neurofibroma (Figure 1). The patient was dismissed with prescriptions for reserpine (Serpasil) and hydralazine (Apresoline); but administration of them was discontinued by his local physician, apparently because they produced excessive sleepiness.

In 1960, at age 10, the patient had blood pressure of 170/110; and reserpine was prescribed again. In January, 1961, right hemiparesis and right facial weakness suddenly developed; but they gradually improved, though a slight right-sided limp persisted. Urinary and blood catecholamine levels again were normal, as were the results of excretory urography and the phentolamine test. The patient was not seen from 1961 to 1968, during which time he intermittently took antihypertensive drugs under the direction of his local physician.

He returned in September 1968 at the age of 18. He felt well and was taking no medicine, but had many café au lait spots and cutaneous neurofibromas (Figure 2). The blood pressure was 180/125. Funduscopy revealed moderate retinal arteriolar narrowing. A loud systolic bruit heard over the abdominal aorta extended laterally toward both flanks, being louder on the right. Skeletal neurofibromatosis was evident in roentgenograms of the cervical and lumbar vertebrae and left sixth rib. Urinary excretion of aldosterone, catecholamines, metanephrines, and vanilmandelic acid (VMA) was normal. An isotope renogram revealed bilaterally equal function. Inulin clearance was 149 ml./min./1.73 sq. m. and para-aminohippuric acid (PAH) clearance was 900 ml./min./1.73 sq. m. An aorticorenal arteriogram revealed high-grade stenosis at the origin of each renal artery, the superior mesenteric artery, and the celiac axis (Figure 3). Renins were obtained after three days on a regimen of 20 mEq dietary sodium and 1.0 gm. of chlorothiazide (Diuril) daily. The value from the low inferior vena cava was 120 ng./L/min. and that from the left renal vein 130 (the sample from the right was lost in a laboratory accident).

Surgery was carried out in October: for stenosis at the origin of the superior mesenteric artery, endarterectomy and Dacron-patch arterioplasty; for stenosis at the origin of the right renal artery, an aorto-renal artery Dacron bypass; and for stenosis at the origin of the left renal artery, a Dacron-patch arterioplasty. The stenosis was tight and fibrous in each instance. Small neurofibromatous masses were spread over the aorta and particularly around the celiac ganglion and region of the renal vessels, and biopsy proved that they were plexiform neurofibromas (Figure 4). Biopsy of the left kidney (Figure 5) disclosed slight changes of the ischemic type.

Postoperatively the patient continued to be hyper-



Fig. 2—(Case 1). Numerous café au lait spots and large neurofibroma in right popliteal space. Thoractomy scar also is visible.

tensive (170/120), and methyldopa (Aldomet) and guanethidine (Ismelin) were prescribed. A postoperative isotope renogram revealed a delayed peak and slowed excretion on the left.

He returned for re-evaluation in April 1969, having taken no medicine for a month. The blood pressure averaged 135/90. There were no abdominal bruits. An isotope renogram revealed bilaterally equal function, definitely better on the left than indicated by the renogram made just after the operation in the preceding October. The results of excretory urography were normal except for some slight atrophy of the upper pole of the left kidney. Creatinine clearance was 137 ml./min./1.73 sq. m.

In April 1970 the patient's blood pressure was 150/100 without medication. Mild arteriolar narrowing but no sclerosis was seen on funduscopic examination. The inulin clearance was 149 and para-aminohippuric acid clearance 660. The findings from excretory urography and renography were unchanged from 1969. Repeat arteriography revealed moderate focal stenosis just distal to the origin of the left renal artery and a patent graft to the right renal artery (Figure 6). There was minimal focal stenosis just distal to the origin of the superior mesenteric artery. An area of possible infarction in the medial aspect of the upper pole of the left kidney was noted again. Urinary excretion of catecholamines, metanephrines, vanilmandelic acid and homovanillic acid was normal. The patient was dismissed with a regimen that restricted dietary sodium but did not

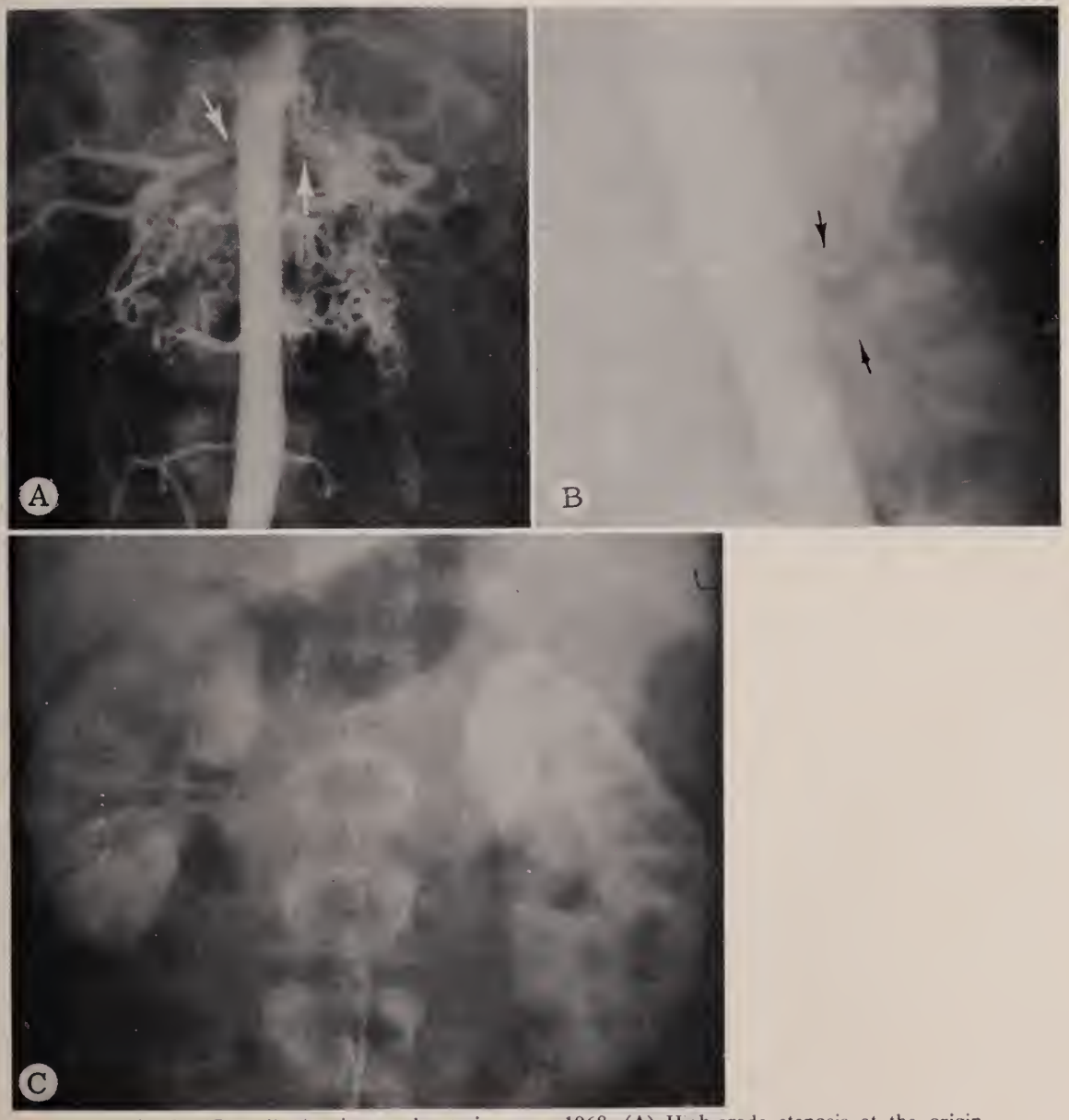


Fig. 3—(Case 1). Aortico-renal arteriograms, 1968. (A) High-grade stenosis at the origin of each renal artery; rich collateral network. (B) Moderate stenosis at origin of celiac axis and superior mesenteric arteries. (C) Nephrographic phase demonstrating both kidneys.

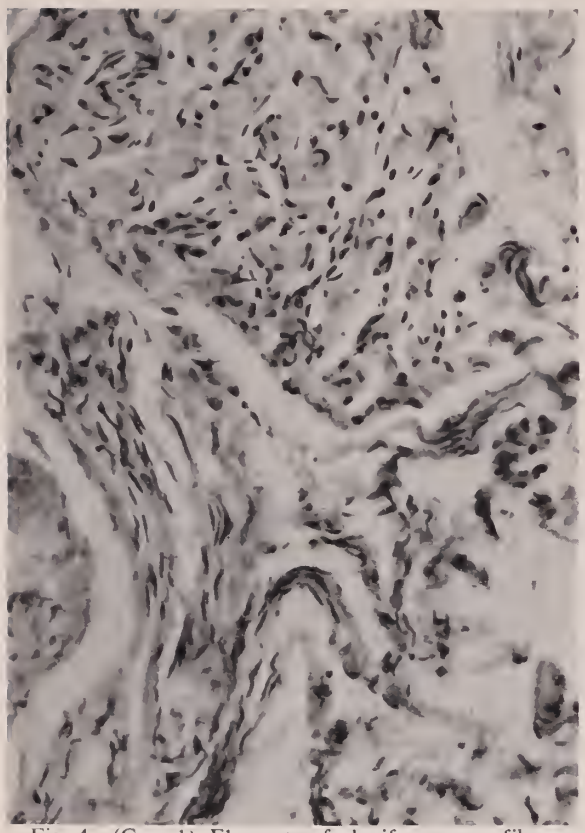


Fig. 4—(Case 1). Elements of plexiform neurofibroma excised from region of renal vessels. (Hematoxylin and eosin; x300.)

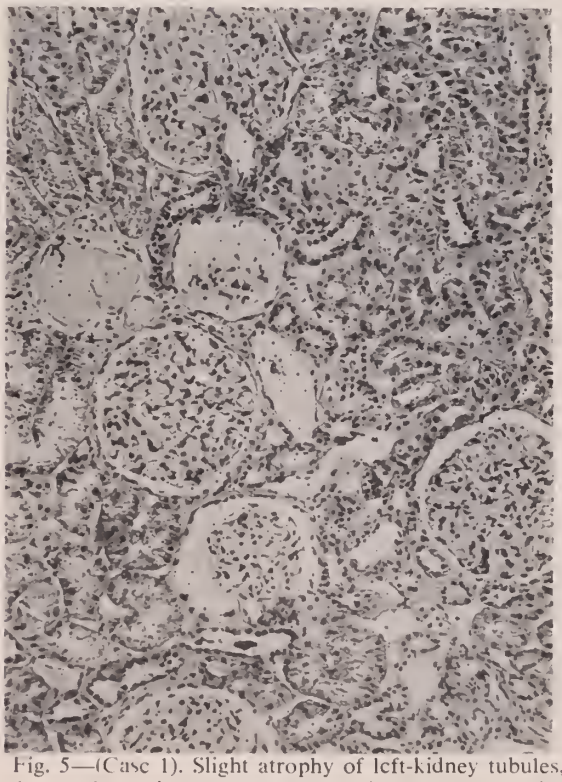


Fig. 5—(Case 1). Slight atrophy of left-kidney tubules, and prominent juxtaglomerular bodies consistent with ischemic change. (Hematoxylin and eosin; x150).

include any drugs. In June 1970 the blood pressure was averaging 125/95 without medication.

Case 2

A 39-year-old white woman was seen in September 1969 because for three years she had been having episodes of occipital headache, diaphoresis, pallor, and palpitations. These began suddenly and usually lasted less than 15 minutes. Transient elevation of blood pressure during the episodes had been recorded. She had had café au lait spots since childhood, and in 1952 a biopsy had confirmed neurofibromatosis. Her mother and one brother were reported to have neurofibromatosis, and three of the patient's children had café au lait spots.

On physical examination the multiple café au lait spots (Figure 7) and neurofibromas were noted. The blood pressure was 129/80. Funduscopy revealed arteriolar sclerosis, grade 1. A systolic ejection murmur, grade 2/6, was heard in the aortic region. During the initial examination two attacks she described as "typical," in which the blood pressure rose to 250/160, were precipitated by palpating the right upper quadrant of the abdomen. A 24-hour urine collection, begun immediately, gave elevated values (numbers in parentheses are upper limits of normal): metanephrines, 34.2 mg. (1.3); vanilmandelic acid, 196 mg. (6.5); homovanillic acid, 19.6 mg. (6.0); and catecholamines, 6,550 μg. (338). A second urine collection confirmed the excess of metanephrines, 22.4; vanilmandelic acid, 44.7; and catecholamines, 2,235. Also the plasma concentration of catecholamines was high, at 21.7 μg./L (5.7 being the upper limit of normal). Creatinine clearance was 105 ml./min./1.73 sq. m. Roentgenographic examination disclosed evidence of neurofibromatosis in the skull and thoracic vertebrae. In the course of nephrotomography, a large mass at the upper pole of the right kidney was demonstrated (Figure 8).

For seven days prior to operation, the patient was given phenoxybenzamine (Dibenzyline), 10 mg. every six hours. Propranolol, 20 mg three times daily, was added four days before surgery; and cortisone acetate, 200 mg., was given for three days and on the morning of the operation.

A well-encapsulated pheochromocytoma, 10.5 by 6 by 3.5 cm., was found in the right adrenal, and the whole gland was removed. The entire specimen weighed 161 gm. Histologic examination revealed typical large polygonal cells (Figure 9). Ganglion-like neural elements, which had been scattered in the pheochromocytomas in several earlier cases where we had noted excessive urinary amounts of homovanillic acid,[1] were not present in the material available for histologic study in this case but may have been contained in the portion used for chemical analysis.

Postoperatively the course was uneventful. The blood pressure was normal and the episodes complained of originally did not recur. In a 24-hour urine collection, the amount of metanephrines was normal (1.2 mg.). In September 1970 she was well and the blood pressure was normal.

Comment

Neurofibromatosis and Pheochromocytoma.

The relationship of pheochromocytoma and neurofibromatosis was first noted by Suzuki[2] in 1910. Mackeith[3], reviewing the literature in 1944, observed that 165 cases of pheochromocytoma had been reported, and that neurofibromatosis had been associated in nine of them. Davis and associates[4] reviewed the literature to 1950 and estimated that the incidence of neurofibromatosis in patients with pheochromocytoma was about 5%, since 10 of 203 patients with pheochromocytoma also had neurofibromatosis.

In 1953 Glushien and co-workers[5] estimated that as many as 10% of patients with pheochromocytoma might have "neurocutaneous syndromes" and suggested that pheochromocytoma, neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, and von Hippel-Lindau syndrome were all of common ectodermal origin and

*See page 32.

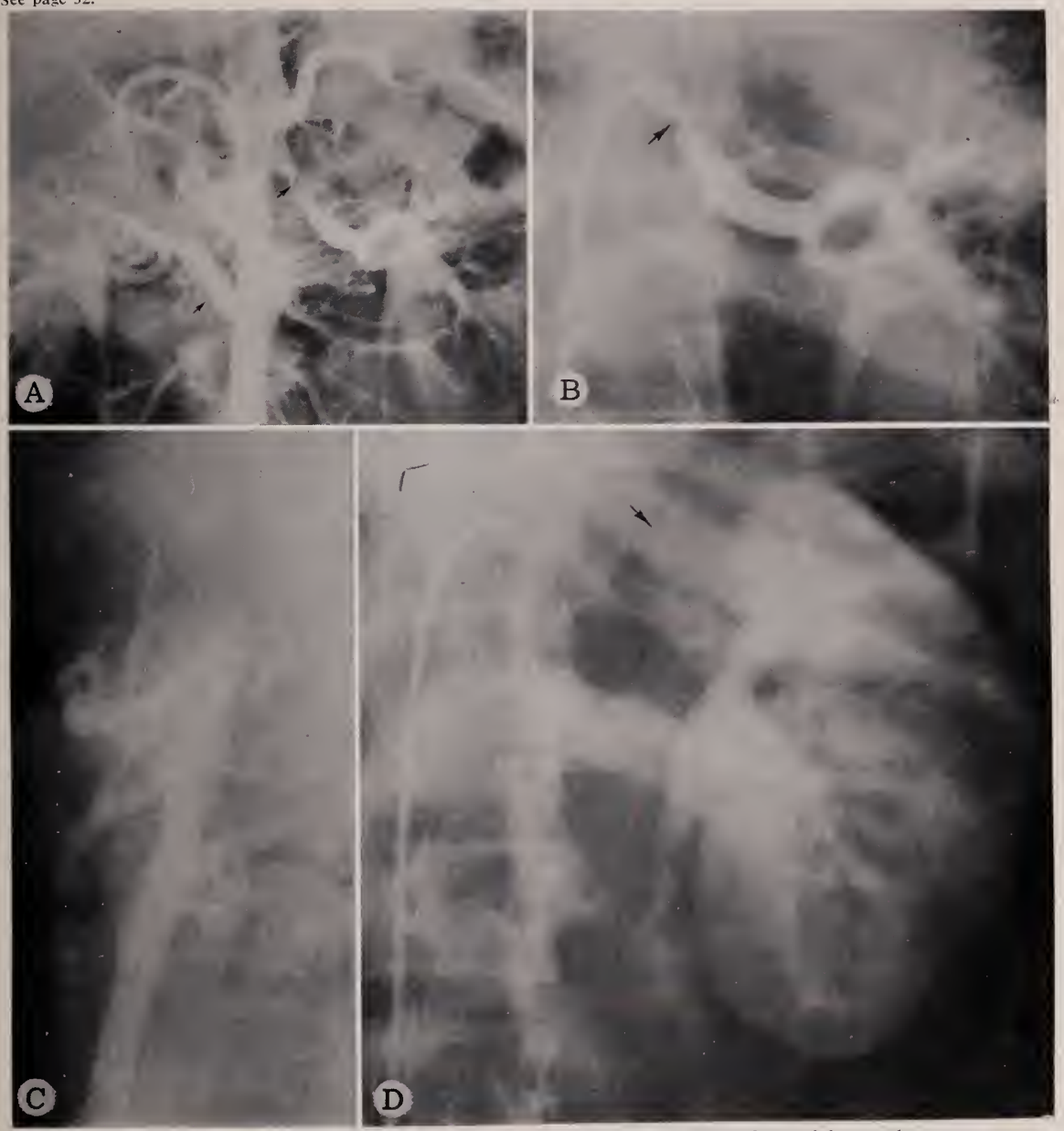


Fig. 6—(Case 1). Aortico-renal arteriograms, 1970. (A) Patent graft to right renal artery; moderate focal stenosis at origin of left renal artery. (B) Moderate focal stenosis of left renal artery demonstrated by selective injection. (C) Minimal focal stenosis just distal to origin of superior mesenteric artery. (D) Late film of selective injection of left renal artery to demonstrate atrophy of upper lobe of left kidney. (Compare with Figure 3 C.)



Fig. 7—(Case 2). Numerous café au lait spots.



Fig. 8—(Case 2). Nephrographic study: large mass at upper pole of right kidney is outlined.

thus likely to appear in combination wih significant frequency. Glushien and associates presented three cases—one of neurofibromatosis and pheochromocytoma and two of neurofibromatosis and von Hippel-Lindau syndrome. In recent years, the association between pheochromocytoma and "neurocutaneous" or other disorders, including medullary thyroid carcinoma, has been noted and discussed by others.[6-16] Schimke and co-authors[17] suggested that this syndrome may represent a possible heritable regulatory defect in the differentiation of chromaffin tissue or neural-crest derivatives. Hermann and Mornex[18] cited remarkable findings in an autopsy series by Schlegel: Among 25,274 cases in 13 years, there were 15 with neurofibromatosis and 23 with pheochromocytoma; and these abnormalities occurred together twice. That is, of the 23 cases of pheochromocytoma, two (8%) included neurofibromatosis; and of the 15 cases of neurofibromatosis, two (13%) included pheochromocytoma. As mentioned earlier, in our series the incidence of neurofibromatosis among patients with pheochromocytoma has been 2.3% and the incidence of hypertension due to pheochromocytoma among patients with neu-

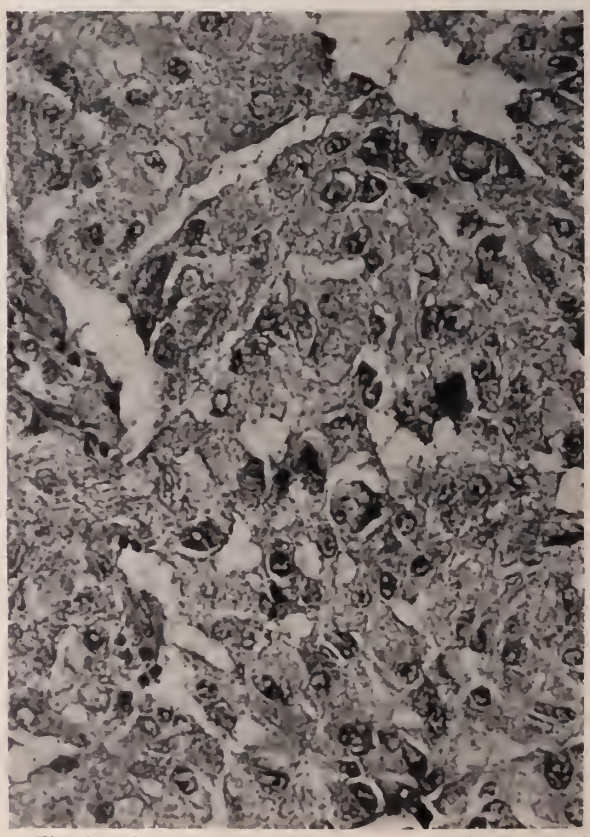


Fig. 9—(Case 2). Pheochromocytoma of right adrenal having typical large polygonal cells with granular cytoplasm. (Hematoxylin and eosin; x350.)

rofibromatosis has been less than 1%.

Neurofibromatosis and Renal-Artery Stenosis

The various renovascular abnormalities reported with neurofibromatosis appear to be a rare cause of hypertension. This relationship has been reviewed fairly recently[19,20]; and two cases since added by Smith and associates[21] and our Case 1 (above) bring the instances of renovascular abnormalities apparently causing hypertension to 15. Of the 15 patients, 14 had neurofibromatosis and one had only café au lait spots. All had renal-artery stenosis or aneurysms, and five had bilateral renal vascular abnormalities. Five had coarctation of the aorta, at least seven had microscopic evidence of neurofibroma or ganglioneuroma in the arterial wall, and three had the pathologic findings of intimal fibrosis, disorganization of the media, and fibrotic changes of the adventitia referred to as "vascular neurofibromatosis."[22,23] Our patient has extensive plexiform neurofibromatosis with bilateral renal-artery and superior-mesenteric-artery stenosis.

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Sturge-Weber Syndrome *

Vascular nevi of the face, scalp, trunk, extremities, and leptomeninges characterize this syndrome. Sturge in 1879, Kalischer in 1897, Lannois-Bernoud in 1898, Parkes-Weber in 1922, Dimitri in 1923, and Krabbe in 1934 each contributed to the knowledge of the complete syndrome. It is congenital, possibly inherited as an irregular dominant character (Givner *et al.*) The facial component is noted at birth while the other features appear in infancy or early childhood.

The cutaneous angiomas are benign, may be telangiectatic or cavernous, have the color of a port-wine stain, and are not elevated. Unilateral facial lesions occur along the distribution of the trigeminal nerve. Conjunctivae, iris, and other parts of the eye and orbit may be involved. Occasionally angiomas extend into underlying fat, muscle, and bone. Postmortem findings in one case revealed similar lesions in the lungs, thymus, spleen, testes, lymph nodes, and pituitary gland (Givner *et al.*) The intracranial angiomas occur in the leptomeninges of the cerebral cortex. Minor foci may be found in the pia, within the underlying cerebral cortex, and in the subcortical medullary substance. Neurologic manifestations include contralateral hemiparesis, hemiatrophy, Jacksonian epilepsy, and mental retardation. Roentgenograms of the skull reveal calcified angioma or localized linear calcification that outlines the cerebral convolutions.

The vascular lesions apparently originate in early embryonic life. Differentation of this syndrome from other cerebral vascular malformations may be made by the presence of the port-wine-colored facial lesions. The prognosis relates to the size and location of the lesion. Successful therapy is limited to small cutaneous lesions. Roentgen therapy in deeper tissues is usually helpful.

Durham, Robert H—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

*See page 27.

Anesthesia

Some years ago a search was made of the records of the Pennsylvania Hospital to see if any account of the first use of ether could be found. The effort was unsuccessful, but Dr. James Darrach of Germantown, who had been resident physician in the hospital in 1846-1847 was still living. He said he could tell about a case which was one of the first, if not the first, in which ether was administered in the hospital. A man was brought in with a crushed leg, which Dr. George W. Norris was going to amputate. Dr. Norris told young Darrach to get some sulphuric ether, saying "We will try what they are doing up in Boston." Neither Dr. Norris nor Dr. Darrach had ever seen it used but young Darrach poured some on a towel and he bade the patient breathe it in.

In a few minutes the man became unconscious and very much alarmed, Darrach called out "Dr. Norris, the patient is unconscious!" Dr. Norris yelled back at him to "take that damned stuff away!"*

Van S. Lawrence, M.D.
Minneapolis, Minnesota

*Anesthesia from Colonial Times by James E. Eckenhoff, BS, MD, FFARCS, J. B. Lippincott Company—1966.

Congenital Diaphragmatic Herniae *

ROBERT R. THOMPSON, M.D.†

THE PATIENT, a full-term female infant, was the product of a normal and uneventful prenatal course in a 25-year-old primipara. (There was no history of drug use or rubella.) During the late second stage there was variability of fetal heart tones. The patient was delivered vaginally by means of outlet forceps.

Infant Examination and X-rays

The infant cried spontaneously. Its color was initially good. Within approximately a minute and a half spasticity was noted and a seizure was thought to occur, manifested by generalized rigidity and oculogyric crisis. When an attempt was made to palpate the heart, it was noted that this organ was displaced to the right. Dextrocardia was initially suspected. The patient was transferred to the newborn nursery isolette where a chest x-ray revealed a large mass of air-filled viscus occupying half of the left hemithorax (Figure 1). The diagnosis was eventration of the diaphragm. An umbilical vein catheter was inserted and sodium bicarbonate was administered intravenously. Also 100 percent oxygen was administered through an ambu bag, using a small amount of ventilatory pressure.

The infant was pronounced dead two hours and twenty minutes after delivery. The remainder of the physical examination revealed no other obvious congenital abnormality.

Necropsy Findings

At autopsy the body was a well-developed, full-term female infant weighing 2740 grams. Abnormal findings were confined to the pleural and peritoneal cavities. The dome of the liver was flush with the costal margins. The left leaf of the diaphragm was completely absent except for narrow ridges posteriorly and anteriorly (Figures 2 and 3). The left chest cavity was occupied by the stomach, pancreas, spleen and entire small bowel and all of the colon up to the splenic flexure. A small portion of the left lobe of the liver was also present in the left chest cavity. The heart was shifted into the right hemithorax;

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*See editorial, page 45.



Fig. 1—X ray. Shows left hemithorax occupied by abdominal viscera in the case presented. Also shows mediastinal shift. Note the complete absence of aerated lung on the left. Taken 20 minutes after birth.

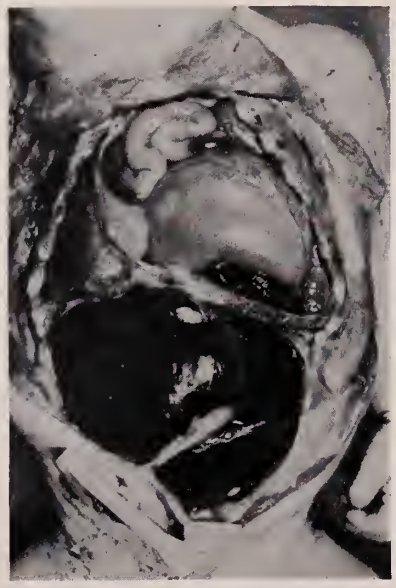


Fig. 2—Autopsy specimen. Shows left hemithorax occupied by abdominal viscera. Note early necrosis of the left lobe of the liver.

it weighed 14.5 gm. and was morphologically normal. The right lung weighed 14.5 gm., the left lung 2.5 gm. The tracheobronchial tree was clear and normal. The left lung was reduced in size to only a small bit of firm, meaty tissue and was completely airless. The right lung was generally atelectatic. The remainder of the organ examination revealed no abnormalities.

Bochdalek Diaphragmatic Hernia

In 1761 Morgagni described the pathology of diaphragmatic hernia;[15] but it was not until 1925 that the first review of the literature was written by Hedbloom. Hedbloom observed that 75% of infants with congenital diaphragmatic hernia died within the first month of life.[12] It was he who first advocated prompt surgical intervention in the treatment of this disorder. The mortality rate has dropped steadily from 78% in 1925 to 10% or less today. Early diagnosis and improved anesthetic techniques account for the improved survival rates.

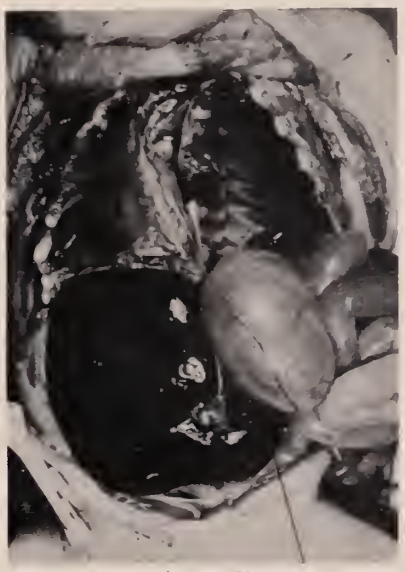


Fig. 3—Autopsy specimen. Shows narrow (rudimentary) leaf of the left diaphragm. Note hypoplastic left lung.

Embryology

Complete separation of the abdominal and chest cavities is a distinctly mammalian characteristic which allows the pleural space to attain the negative pressures necessary for respiration.

The intact diaphragm is a fibro-tendinous muscular organ which derives from two sources. Anteriorly it is formed by the septum transversum, which ultimately becomes the central tendon of the diaphragm. The lateral portions of the diaphragm are formed as the lung buds push dorsolaterally, invading the embryo body wall.[1] The failure of this membrane to unite with the muscular central portion is responsible for the patent pleuro-peritoneal canal or Foramen of Bochdalek.

Complete Agenesis Unlikely

The diaphragm is not a "paired organ" which developes in the midline, but a composite organ whose final structure is the result of a "bulldozing" process which goes on inside the peritoneal and pleural cavities. Therefore, complete agenesis of the diaphragm or of a hemi-diaphragm is un-

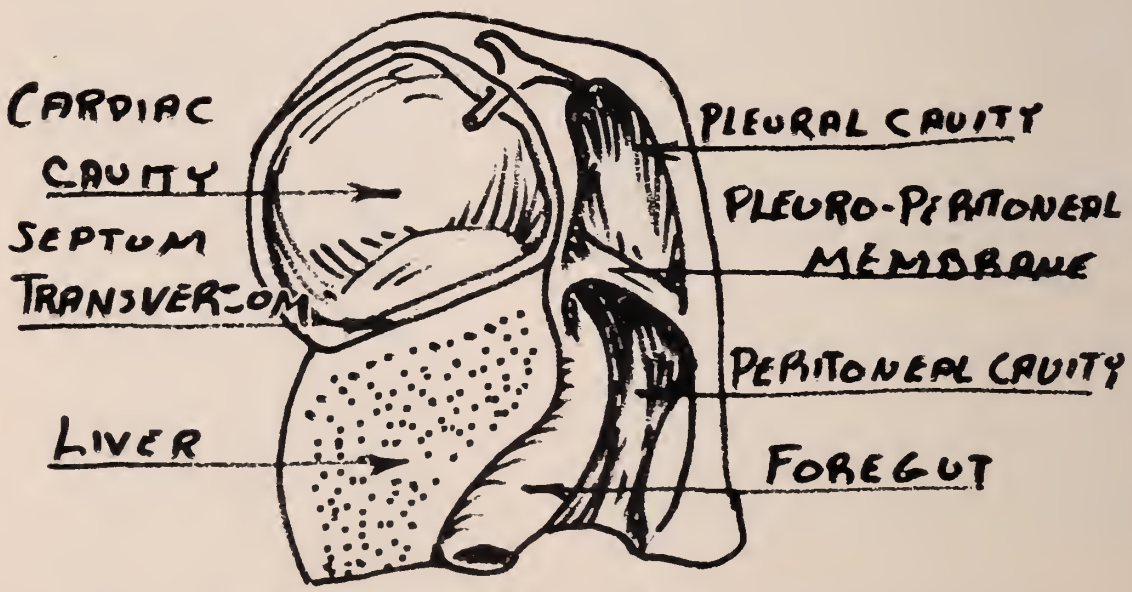


Fig. 4—Drawing. Taken (modified) from Arey. Shows seven-to-eight week embryo and depicts the pleuroperitoneal membrane through which herniae of Bochdalek occur. Shows the relation of this membrane to the septum transversum.

likely to occur. The central hemi-diaphragmatic defects are thus apt to be ones of degree rather than of kind.

Incidence

Adkins reports the incidence as one in every 2,000 births.[3] The left hemi-diaphragm, for reasons which are only speculative, is involved approximately four times as often as the right side.[2,1] For equally obscure reasons, there seems to be a slight preponderance of male babies afflicted.

Usually No Sac

If the abdominal viscera are pushed through the pleuroperitoneal foramen prior to its closure but after the pleural and peritoneal layers are formed, the hernia will have a true sac. Usually it does not.

Lung Truly Hypoplastic

The ipsilateral lung is truly hypoplastic, which undoubtedly contributes significantly to the mortality of this condition.[6]

Other Types of Concenital Diaphragmatic Herniae

The locations of the types of congenital diaphragmatic herniae are shown diagrammatically in Figure 5.

Esophageal Hiatal Hernia

This particular hernia, sometimes called *congenitally short esophagus,* represents the most common form of congenital diaphragmatic hernia. It occurs when the stomach is slow to descend into the abdominal cavity and is either trapped above the diaphragm, or enlarges the esophageal hiatus. Vomiting begins in the first two weeks of neonatal life, and in 50% of the cases, there is hematemesis and attendant anemia in 25% of the cases. Surgical correction is reserved for these patients who fail to respond to upright positioning and bland dieting.

Hernia of Morgagni

The Hernia of Morgagni comprises 3 to 5% of the congenital diaphragmatic hernia and occurs

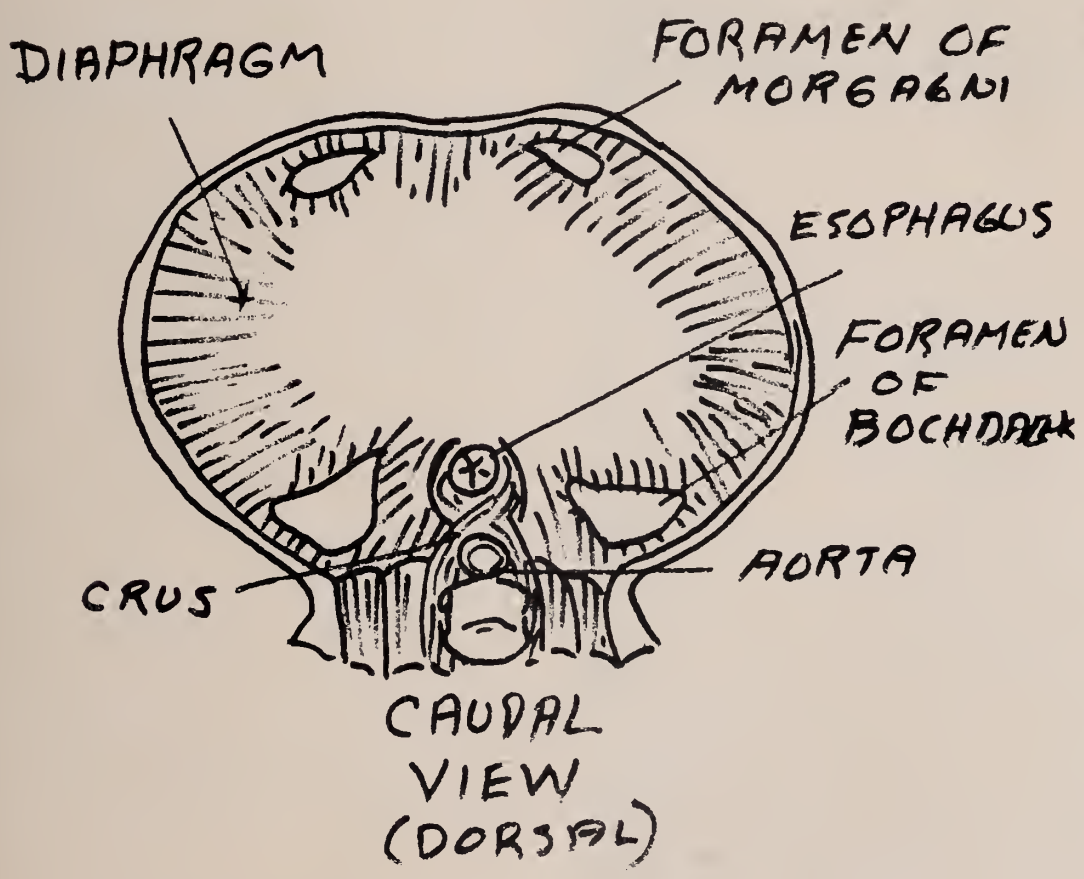


Fig. 5—Shows diagramatically the different locations of the types of diaphragmatic herniae from the under surface of the diaphragm.



Fig. 6—X ray. Barium swallow illustrates a thoracic stomach in a six week old infant who was asymptomatic.



Fig. 7—12-year-old asymptomatic patient showing eventration of the left hemidiaphragm.

through *Larrey's space,* the gap between the zyphoid and the coastal-diaphragmatic junction. Of all the congenital diaphragmatic herniae, it is most likely to remain asymptomatic until later life. The defect is easily approached surgically from an abdominal exploration when the preoperative diagnosis is well established.

Eventration of the Diaphragm

This anomaly does not represent a true hernia, but rather varying degrees of elevation of a thin leaf of a poorly reinforced hemi-diaphragm. Ventilatory distress may occur, but usually the condition is asymptomatic (Figure 6 and 7). X-rays reveal a smooth pleurodiaphragmatic interface with normal movement of the diaphragm.

The majority of patients are treated nonoperatively. Diaphragmatic imbrication of plication is the treatment where treatment is indicated. Occasionally differentiation from a Bochdalek hernia is crucial but difficult. Pneumoperitoneum, if time permits, may aid in the distinction.

Bochdalek Hernia

Symptoms of a foramen of Bochdalek hernia may be catastrophic in onset shortly after birth. They include dyspnea, cyanosis, and usually a scaphoid abdomen. Marked mediastinal shift may be mistaken for dextrocardia. Peristalsis over the chest cavity is an unreliable diagnostic sign.[3,2,6]

Early diagnosis and surgical correction of this condition are imperative. Loss of "right of domain" of the abdominal organs may prohibit layered closure of the abdominal wall until the skin and subcutaneous tissues have stretched, necessitating a two-stage closure.

Summary and Conclusion

The incidence of *all* types of congenital diaphragmatic hernia would seem to approximate one in 2,000 live and stillbirths. Respiratory distress, apnea, cyanosis, apparent dextrocardia, scaphoid abdomen and persistent vomiting are signs which should alert the clinician to the diagnostic possibility of a congenital diaphragmatic hernia, especially during the first 72 hours of life. Early surgical management of some types of symptomatic congenital diaphragmatic hernia may be imperative.

*See page 74 for references.

Duplication of the Duodenum

Presenting as an Adrenal Tumor

DAVID J. DUNLAP, M.D.,* JAMES M. MILLER, M.D., ROBERT G. McCANDLESS, M.D.

DUPLICATIONS OF THE small bowel occur most frequently in the ileum and almost always near the mesenteric border.[1] Bremer has written a comprehensive paper which includes the many theories for the formation of intestinal duplications.[2] He feels that true duplications always contain all the tissue layers of the intestine. He further states that in cystic type duplications, the original type of mucosa may change and resemble gastric mucosa or may be partially destroyed by internal pressure. Jalenko reported a case of duodenal duplication in which parietal cells were found in the specimen.[3]

In 1966 Houston and Lynn found less than 30 cases of duodenal duplications reported in the literature.[4] Gross has reported one case of duodenal duplication occurring on the antimesenteric side of the duodenum.[5]

Case Report

A thirteen-year-old boy was admitted to the Sandia Base Army Hospital on March 20, 1968, for evaluation of a right adrenal mass. He had been seen in the Urology Clinic at the Sandia Base Army Hospital because of enuresis. Other urinary symptomology included occasional urinary urgency and dark spots on his undershorts. An intravenous urogram had shown normal kidneys and ureters, but definite enlargement of the right adrenal shadow.

Physical examination revealed a normotensive male with no physical abnormalities. There was no palpable adrenal mass. The urinalysis, complete blood count, sedimentation rate, BUN, serum electrolytes, serum creatinine, creatinine clearance, urinary electrolytes, urine culture, urinary vanilmandelic acid, urinary 17-ketoid steroids, 17 ketogenic steroids, and pregnanetriol were normal. A voiding cystourethrogram was normal. On the 4.5-cm. cut a nephrotomogram showed a triangular-shaped right adrenal mass approximately 2.5 x 3 cm. in size. A percutaneous right femoral aortogram revealed normal renal vasculature and no vesesls in the area of the adrenal mass.

On March 21, 1968, both kidneys and adrenal glands were explored transperitoneally through a cheveron-type incision. The left colon was reflected and the left kidney and adrenal were normal. The right colon was reflected medially; the right kidney was normal but there was a 3.2 x 2 x 2-cm. mass in the areas of the right adrenal gland with a smaller nodule slightly medial to this, measuring approximately 0.5 cm. in diameter. The smaller mass was loosely adherent to the second portion of the duodenum, with numerous fibrous adhesions to the undersurface of the liver. The entire tumor mass was dissected free and removed. There was no communication with the duodenal lumen.

Gross pathological examination of the removed specimen showed two cystic structures which contained viscous chocolate-colored fluid and inspissated and calcareous debris.

Microscopic sections revealed multiple portions of normal-appearing adrenal cortex, fibrous tissue, hemorrhage and calcification. Also included were sections showing a complete gastrointestinal wall with the mucosa resembling small intestinal mucosa but containing large numbers of parietal cells. The specimen was examined at the 4th U.S. Army Medical Laboratory at Fort Sam Houston, Texas, and at the Armed Forces Institute of Pathology, Washington, D.C.

Discussion

Cysts of the adrenal gland usually are pseudocysts resulting from cystic degeneration and may contain blood and calcareous debris.[6] A duplication of the duodenum presenting as an adrenal tumor is an unusual entity, but certainly possible considering the proximity of the right adrenal gland and the second portion of the duodenum. Because of the presence of all layers of the bowel wall in this case, a true duplication must be considered. Both antimesenteric duodenal duplications and the presence of parietal cells in small bowel duplications have been previously reported.

*Sandia Base Army Hospital, Albuquerque, New Mexico. Now practicing urology in Minneapolis, Minnesota.

Summary

A case is reported of a 13-year-old boy with a mass in the area of the right adrenal gland. This mass was presumed to be a duplication of the duodenum invading the adrenal gland.

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1. Demeulenaere, L.: Action du R 1132 sur le transit gastro-intestinal, Acta gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.

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The New Editor Appreciates the Old

A NEW EDITOR of an old journal should look backward before leaping ahead into the uncharted future. Although MINNESOTA MEDICINE existed in bulletin form and as a supplement to other publications in the late nineteenth and early twentieth centuries, its birth as an independent journal can be fixed as of January, 1918, when Volume One Number One was published under the editorial direction of Dr. Carl Drake. For three and a half decades he continued as editor to be succeeded by Arthur Wells, the great pathologist of Duluth. Then in 1961, Dr. Carl Rice was named editor-in-chief. Thus in 53 years MINNESOTA MEDICINE has been under the direction of three men.

As the incoming editor my first duty, a pleasant one, is to pay tribute to Carl Rice, who now becomes, with this issue, Editor Emeritus. MINNESOTA MEDICINE under his able direction has become recognized as an outstanding state medical journal, the winner of many awards for excellence. He has earned the thanks of the medical community and of the state for a superior performance over the last 11 years, his term as editor-in-chief. I will not attempt to assess his work now. A proper appreciation of Carl Rice's contributions will be set forth in a later issue. As editor he has set high standards for others to follow. The Editorial Board's first objective is to find what other physicians around the state would like to join the Board and take part in the exciting venture of publishing MINNESOTA MEDICINE and the editor would like to hear from such interested people.

As Carl Rice has frequently stated, MINNESOTA MEDICINE can be a great medical journal. Minnesota is known as an outstanding medical center. Its medical school in Minneapolis and the Mayo Clinic in Rochester are acclaimed throughout the civilized world. Minnesota's other medical schools soon to open in Rochester and Duluth are surely destined for greatness. In our state in practically every field of medicine can be found world-renowned experts. But the pages of MINNESOTA MEDICINE are not only open to the experts but to every physician who wishes to address this audience. The editor appeals to the readers for contributions, for articles, case reports, and letters.

Your new editor is no stranger to this masthead having been put there on Carl Rice's recommendation in 1961. The average tenure of the first three editors was 17⅔ years. To meet this average I would have to live to be an octogenarian.

Reuben Berman, M.D.
Editor



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The White Doctor—Black Patient Relationship

It is my contention that in the diagnosis and treatment of the ills of-the-black-patient-the-white-doctor often fall short of the high level of competence that he usually achieves in treating his white patients. This is, of course, a generalization, and unquestionably there are many notable exceptions. Nevertheless, if the premise is true, it is something that we in the medical profession should try to correct.

Let us assume that there are some markedly prejudiced white physicians who come into contact with black patients and frankly give them second-rate treatment. Although in this geographic area I feel the number of physicians who would do this is small, this group should be mentioned only to be condemned. On the other hand, there are many physicians who might even go the extra mile, so to speak, with their black patients if it were not for several mitigating factors that come into play, and it is to these I would like to address myself.

The problem of communication so necessary to the establishment of a good patient-doctor relationship may be hampered by a lack of comprehension on the doctor's part. He simply doesn't understand or misunderstands the patient's complaint, because of a language barrier. The idioms of black culture are often unknown to him, and thus he may miss the subtle or not so subtle [tip off] to the crux of the matter. Hence, he fails to diagnose the case in his usual efficient manner, and at the very least, subsequent visits and more cost will be required in order to pinpoint the problem. At the worst the problem will go undiagnosed. On the other hand, the patient may not understand the doctor's question, and his answer could well be completely opposite to the actual facts. Thus the doctor will be thrown off track. Either the doctor, or his patient, or both, might realize their lack of understanding but not want to admit it—for the same reason, false pride or vanity.

The second problem that may exist is a lack of rapport between the two. Although this exists in the white-white situation, it undoubtedly is more prevalent in the white-black situation. Is it a lack of trust in each other? Is it disrespect for the other's race? Is it that each suspects the other of "putting one over on him?" For whatever the reason, if the lack of rapport exists, only the most superficial of problems will be adequately dealt with, and the experience will only serve to make future confrontations more difficult. If an uncomfortable relationship exists between the doctor and his patient, each may subconsciously leap to accept the superficial problem with its solution as a completion of their contract with each other. Hence, the deep problem, perhaps the life endangering problem, goes unsolved and untreated.

I have not mentioned the openly hostile black, because I think it takes only the most dire of circumstances for him or her to come to see a white doctor in the first place. In all but the purely mechanical parts of medicine mutual respect for each other is a must for a satisfactory patient-doctor relationship to exist. The doctor cannot assume all fault in this unhappy situation should second-rate treatment result.

There are several steps a physician could take to help rectify an inequality in his practice: First, help his black patients feel more at home by having at least a few copies of black literature in his reading rack and perhaps an object or two of black art in his waiting room or office. Second, the distribution of a booklet to patients with common phrases used by physicians and what they really mean. Both white or black patients might benefit by this clarification of terms. A third helpful step might be to openly admit to the patient that I, as his doctor, cannot really understand what is going on and admit that it may be my own fault. This is hard to do sometimes especially when we are rushed for time or uncomfortable in our relationship. Fourth, ask our black physicians in this area to discuss the matter with us in a lecture or in a group discussion.

Finally I think that both we as white physicians and the blacks as patients should admit that we are simply not as comfortable with each other as we should or could be. It will take an open line of communication between each other if we are to break down some of these barriers. Great relationships can only exist where there is honesty, openness, and trust between participants, and I just doubt if this commonly exists between the

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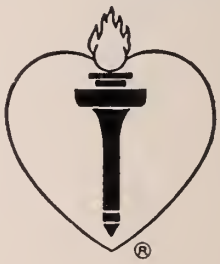
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white doctor and his black patient. It is my feeling as a white physician that it is a very special privilege and responsibility for me to take care of a black patient. I realize that although I might wish to cast off all racial predjudices one just dues not shed his past experiences; they are there and they always will be there. It is only with the making of new and enlightening experiences that the old will cease to have an effect on my actions. I think we should welcome the challenge of the white doctor-black patient confrontation and work to make it a satisfying experience for both.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Diaphragmatic Hernia*

DIAPHRAGMATIC HERNIA represents the most urgent surgical emergency of the newborn. Anoxia and respiratory acidosis develop rapidly and may lead to a fatal outcome in a remarkably short period of time.

Early detection is obviously essential to survival but, in the Mayo Clinic's experience, the fatal cases have been largely in the group diagnosed and operated upon within six to eight hours of birth. Obviously there are many factors at work which are beyond the physician's control. Early examination may be combined with early treatment even before a diagnosis is made.

Administration of oxygen, insertion of a nasogastric tube to delay gaseous distention, and providing a warm, humid environment (Isolette) are the most immediate needs. Gentle respiratory support by means of an endotracheal tube is the next consideration. The intravenous administration of sodium bicarbonate is an essential step in combatting the developing acidosis. However, this alone will not adequately correct the acidosis and certainly will not save the infant who develops distress early.

Surgery must be as immediate as possible. Opening the abdomen and relieving the pressure of the abdominal viscera against the lung and mediastinum is the indicated treatment. Once this has been accomplished the patient may show remarkable improvement. No attempt should be made to fully expand the ipsolateral lung. Hypoplasia and atelectasis respond better to slower and more gentle expansion.

In the event that the patient's condition is still precarious and the abdominal tension seems too great on closure, the use of Silastic-backed Teflon to create a ventral hernia or "silo" is a most effective way of temporizing.

Early diagnosis and immediate surgery offer the only chance for survival of these critical cases.

Hugh B. Lynn, M.D.†
Rochester, Minnesota

*See page 33.
†Pediatric Surgery; Mayo Clinic, Rochester.

Reminder

119th Annual Meeting of the Minnesota State Medical Association in Rochester, Minnesota, May 18, 19 and 20, 1972.

The teenager today lives in a mighty confusing world. Half the grownups are telling him to find himself while the other half tell him to get lost.

Polymyalgia Rheumatica

THE REPORT, "Polymyalgia Rheumatica" by Molldrem and Olin* is noted with particular interest because it again calls attention to the relationship of polymyalgia rheumatica to giant cell arteritis and the importance of early diagnosis and therapy of these conditions. It has been our experience that these syndromes will be found more frequently when the clinician is aware of the possibility of this condition. Involvement of the coronary arteries by giant cell arteritis also has been suspected by us. While very few cases have been demonstrated at autopsy, surgeons doing revascularization procedures of the myocardium can help establish this diagnosis by getting biopsy material when this condition is suspected.

It should be pointed out again that the temporal artery biopsy may be negative. Temporal arteritis is known to be patchy in "skip" areas so that a negative biopsy does not exclude the disease. The etiology of these syndromes remains unknown, but as immunological investigations are carried out, we may expect in the future to come closer to having this problem solved.

At the present, we should have a high index of suspicion, keeping in mind that this may be the diagnosis in patients over fifty-five years of age with girdle muscular pains, elevated sedimentation rates and with or without temporal arteritis. It should also be remembered that the natural course of the disease is from three to five years or longer and that therapy with steroids may have to be prolonged.

Harold E. Miller, M.D.
Minneapolis, Minnesota

*See page 19.

Cover Photograph

"Mount Fujiyama"

While attending the 1969 International Congress of Radiology in Japan, Dr. Harry W. Mixer took the cover photograph of Mount Fujiyama. He used ektachrome color film and took the shot of Fujiyama early in the morning. Dr. Mixer indicated that on the previous day the Mountain was completely obscured by clouds, but on the morning of the picture taking, the clouds had all disappeared and there Mount Fujiyama stood in all its majesty.

Mount Fujiyama located in south central Honshu is the highest mountain in Japan.

Dr. Mixer is a radiologist practicing in the Minneapolis area.

The surgeon now ordered his patient to be stripped to his shirt, and then entirely baring the arm, he began to stretch and examine it, in such a manner that the tortures he put him to caused Jones to make several wry faces; which the surgeon observing, greatly wondered at, crying, "What is the matter, sir? I am sure it is impossible I should hurt you." And then holding forth the broken arm, he began a long and very learned lecture of anatomy, in which simple and double fractures were most accurately considered; and the several ways in which Jones might have broken his arm were discussed, with proper annotations showing how many of these would have been better, and how many worse than the present case.*

*Henry Fielding: Tom Jones Book IV, Chapter XIV, 1749.

Letter to the Editor

Teenage Mothers

In the September issue of "Minnesota Medicine*" Doctor Eric Knox reported on a group of 120 girls, age 12 to 16 years, who were delivered of full-term pregnancies at Hennepin County General Hospital in the years 1968 and 1969. The author compared the complications in this group with the complication rate of all age groups and found that in the young teenager the risks were higher, the baby required more specialized attention, and there were more Cesarean sections, a higher incidence of toxemia, prolonged labor, premature delivery, and post partum hemorrhage. Twenty-five percent of the infants were placed in the high-risk nursery.

Of the 120 girls delivered in 1968 and 1969, 26% were married, but 96% of these marriages took place *after the pregnancy was diagnosed.* The author closes by pointing out three facts to his fellow pediatricians: (1) The young mothers are themselves pediatric patients, and as such, need specialized care; (2) 25% of the infants are in the high-risk group and perinatal mortality runs higher and (3) 75% of the mothers are keeping their children of which only 25% of these receive adequate care.

The article ends with a timid suggestion that "studies are needed to define the role of contraception in the professional approach to the teenage female."

The chilling truth is that probably 99% of these 120 pregnancies were *compulsory pregnancies,* forced upon individuals who are but children themselves. Only 26% got married. There is no follow-up given of the social results of these marriages, but the instability of early teenage marriages is an apparent social fact. Twelve percent of these girls received no prenatal care at all, probably because of shame, ignorance, or lack of funds.

The author never questioned the morality of allowing these children, still almost helpless in the jungles of our modern society, to go through the physical risks, discomfort, humiliation, and anguish of a compulsory pregnancy. He only examined the increased incidence of risks and suggested greater vigilance in the care of these patients.

I frequently see this age group in my own obstetrical practice. I have had to face them week after week in the office, watching them gradually become old before their time—hurt and disillusioned by the world around them—withdrawn from their contemporaries, yet not adults, watching the distortion of their young bodies before they themselves are fully grown.

And, in addition to guiding these young mothers through a high-risk pregnancy, I must deliver a child which will probably (75%) receive inadequate care!

One more point of concern to me is the fact that there were no therapeutic abortions performed at Hennepin County General Hospital for any reason during the two years in which this study was carried out, and it is almost a certainty that there were some cases of pregnancy from rape and incest during this period of time. Were they either included in this group of 120 girls, or were they turned away to seek help elsewhere?

A recent annual report from the Minnesota State Department of Public Welfare for 1970 includes 194 known cases of child abuse in 1970, 17 of which were cases of incest. Hennepin County was responsible for 37.1% of these cases. I am aware of two cases of incest in the past two months, both in 13-year-old girls—one impregnated by her 17-year-old brother and the other by a contrite father. Both girls were brought to St. Paul Ramsey County for help. Did Hennepin County General have no such cases in two years, or were such included in the group of 120?

I submit to you that this is an immoral situation. I would not force a daughter 16 years or less through a compulsory pregnancy, no matter what the circumstances of conception. And the same compassion should exist for the underprivileged.

Jane E. Hodgson, M.D.
St. Paul, Minnesota

*Page 701.

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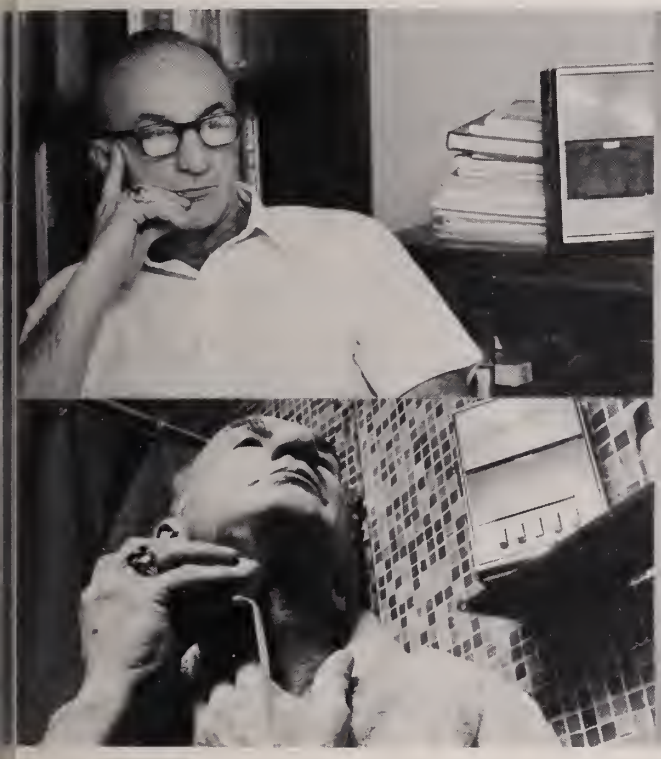
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(Continued to page 58)

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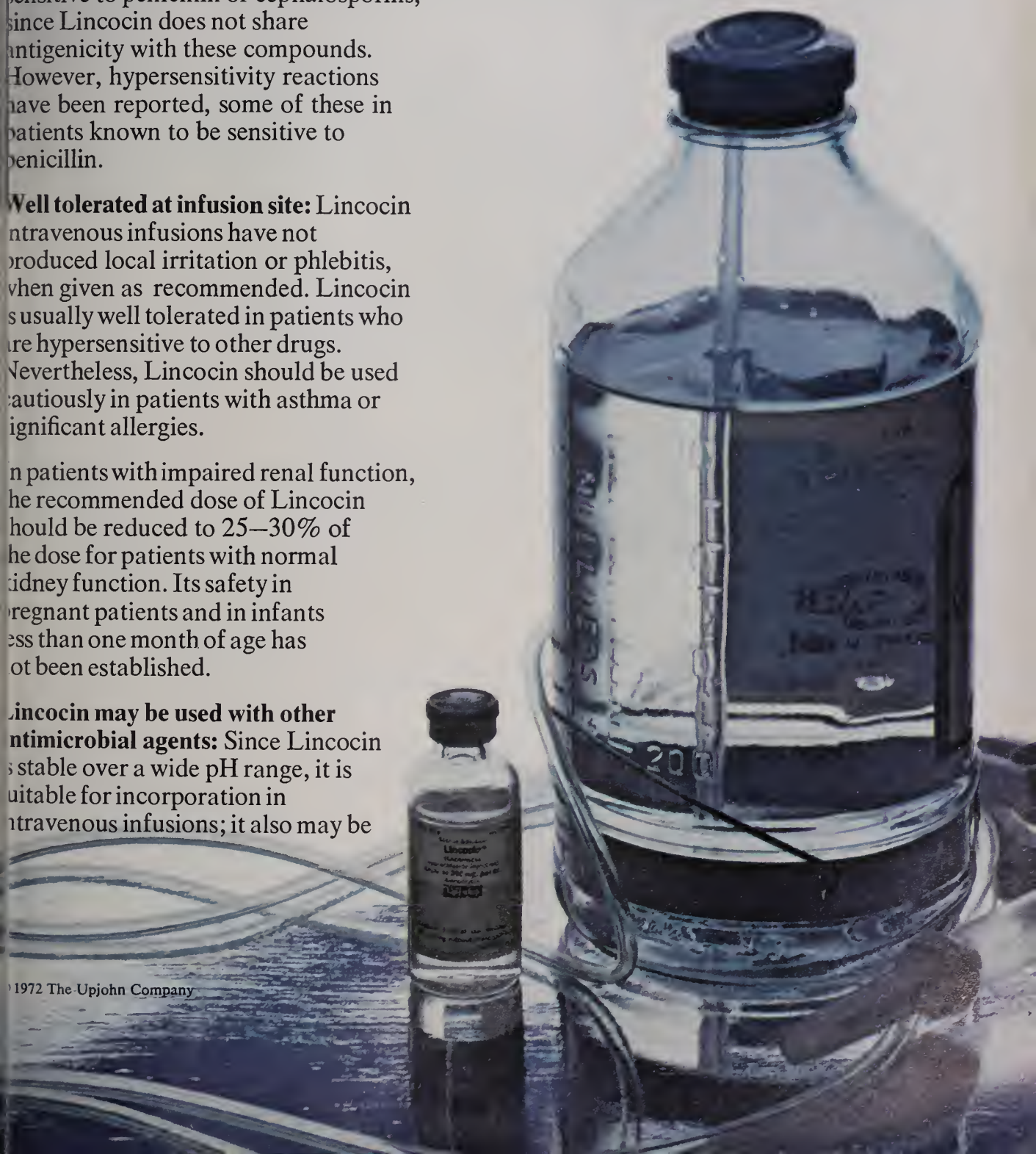
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Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

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Laboratory Medicine

Hepatitis Associated (Australia) Antigen

JEFFREY McCULLOUGH, M.D.* AND HERBERT F. POLESKY, M.D.†

In 1964, Blumberg[1] found a new antigen when studying sera from multitransfused patients for isoprecipitins against lipoproteins. Since an antibody present in the serum of two hemophiliacs reacted with the nonlipoprotein antigen in serum from an Australia aborigine, he and his coworkers[2] called it the Australian antigen. Subsequently, the antigen was found in patients with mongolism, leukemia, leprosy and most recently polyarteritis nodosa[3,4,5]. An association between Australia antigen and hepatitis became apparent when a previously negative patient with Downs syndrome developed Australia antigen positivity concurrent with hepatitis.[5] Studies too numerous to review here confirmed the association of Australia antigen with hepatitis and resulted in its being renamed the hepatitis-associated antigen.

In addition to widespread publicity of studies of hepatitis-associated antigen, hepatitis has been mentioned frequently in the press because of the epidemiologic reports on the increased incidence in individuals between 15-30 years of age and its association with drug usage.[6] Further publicity has resulted from recent court decisions in cases of transfusion associated hepatitis that have accepted the doctrine of strict liability[7] and applied the concept of implied warranty to services.[8] Thus it seems appropriate to review current knowledge of the hepatitis-associated antigen and to present data on its incidence in Minnesota blood donors.

Characteristics of the Antigen

Although the exact nature of the antigen and its relationship to hepatitis is unsettled, present concepts are as follows:

Hepatitis-associated antigen is a virus-like particle. Evidence for this includes: (a) its appearance by electron microscopy;[9] (b) the presence of small amounts of RNA[10] and RNA dependent DNA polymerase activity[11] in isolated preparations of antigen and (c) the detection of hepatitis-associated antigen by fluorescent antibody in the nuclei of liver cells of patients with hepatitis.[12] Evidence against its being a virus includes failure to obtain growth in tissue culture and the fact that hepatitis-associated antigen is not present in cord blood of infants whose mothers are hepatitis-associated antigen positive.[13]

According to the National Research Council[14] "the detection of hepatitis-associated antigen in a person's serum is a specific indication that the person is infected with one of the causative agents of human viral hepatitis." Supporting studies include Giles et al.[15] who found a 95% incidence of hepatitis-associated antigen in (MS-2) long incubation hepatitis and 0% incidence in (MS-1) short incubation hepatitis. The frequency of hepatitis-associated antigen positivity[16] is generally greater in parenterally acquired hepatitis (13-95%) than cases considered infectious (0-47%). *The variability and overlap of these figures should be kept in mind when hepatitis-associated antigen is used as a diagnostic test.*

Role in Etiology of Acute Hepatitis

The etiologic role of hepatitis-associated antigen in serum hepatitis is also supported by transfusion studies. Gocke et al.[17] reported that nine of twelve recipients of hepatitis-associated antigen positive blood developed hepatitis and seven of these patients became hepatitis-associated antigen positive; however, subsequent studies indicate that the hepatitis risk of hepatitis-associated antigen positive blood may be 50%[18] or lower.[19] The incidence of hepatitis among recipients of hepatitis-associated antigen postive blood is three to five times that of recipients of blood negative for hepatitis-associated antigen[14] and hepatitis-associated antigen is 85 times more common in blood donors implicated in hepatitis transmission than in normal controls.[20] In cases of transfusion associated hepatitis in Minneapolis, six of thirteen (46%) recipients developed a positive test for hepatitis-associated antigen: however, only one of the 171 (0.59%) tested implicated donors was hepatitis-

*Assistant Professor Laboratory Medcine; Director, Blood Bank, University of Minnesota Hospitals; Medical Director, St. Paul Regional Red Cross Blood Center.
†Director, Minneapolis War Memorial Blood Bank; Assistant Professor Laboratory Medicine, University of Minnesota.

associated antigen positive when tested retrospectively. Taswell et al.[20] have shown an excellent correlation between the incidence of hepatitis-associated antigen in the donor population and the frequency of transfusion-associated hepatitis. This seems to hold for Minneapolis where hepatitis occurs in 1/1670 recipients and 1/1610 donors is hepatitis-associated antigen positive (Table 1).[21]

TABLE 1

Hepatitis-Associated Antigen Testing on Patient Specimens*

Diagnosis	# tested	# positive	%	# with antibody
Hepatitis	151	57	(37.7)	0
Possible hepatitis	76	6	(7.9)	0
Close contact with hepatitis	40	3	(7.5)	0
Patients on Methadone	56	2	(3.6)	1
Specimens submitted without a diagnosis	342	39	(11.7)	1
Other†	100	0		2

*Specimens sent to the Minneapolis War Memorial Blood Bank for hepatitis-associated antigen testing. To enhance sensitivity specimens were concentrated with lyphogel.
†Hospitalized patients with miscellaneous diagnosis.

The appearance of hepatitis-associated antigen in a patient's serum is usually transitory and may occur up to four weeks prior to clinical or laboratory evidence of liver disease.[16] Hepatitis-associated antigen usually disappears before symptomatic or liver function recovery. From 18-35% of hepatitis-associated antigen positive patients have remained hepatitis-associated antigen positive after 24 months, and it appears that chronic hepatitis-associated antigen positivily occurs more commonly following mild or subclinical hepatitis. Thus, the "carrier" may be unaware of preceding illness, an important point in blood donor screening.

In acute hepatitis, hepatitis-associated antigen testing identifies patients with "hepatitis-associated antigen positive hepatitis" (Table 1). A positive test suggests a viral etiology, infection by parenteral transmission (though large doses of orally administered MS-2 can cause hepatitis-associated antigen positive hepatitis)[15] and a more prolonged hospital course. Such patients should be cared for with isolation techniques. A negative test for hepatitis-associated antigen does not rule out viral hepatitis. Patients developing hepatitis in point source epidemics have been uniformly hepatitis-associated antigen negative. In classical short incubation (infectious) hepatitis, hepatitis-associated antigen is usually not present though other virus-like particles have been observed.[22] *Because of the lack of sensitivity of present methods and the transient presence of hepatitis-associated antigen, many cases of serum hepatitis will be hepatitis-associated antigen negative.*

Relationship to Chronic Liver Disease

The status of hepatitis-associated antigen in chronic liver disease is somewhat less clear. Wright[23] reported that 50% of patients with "unresolved classic hepatitis" were hepatitis-associated antigen positive, and Fox[24] found 40% of seven patients with "prolonged viral hepatitis" to be hepatitis-associated antigen positive. Other forms of chronic active hepatitis have a much lower rate of occurrence of hepatitis-associated antigen and cirrhosis (including crytogenic, inactive post-necrotic and biliary) is usually hepatitis-associated antigen negative. A few cases of hepatoma have been reported to be hepatitis-associated antigen positive.[25] Thus, in chronic active hepatitis, hepatitis-associated antigen testing appears to differentiate between two groups, a "hepatitis-associated antigen positive group that most likely progressed from acute viral hepatitis, and the lupus erythematosis positive, hepatitis-associated antigen negative group that probably represents an immunologic aberation."[16]

Antibody Studies

Antibody to hepatitis-associated antigen when detectable, occurs about four to five weeks after transfusion of infectious plasma although we have found it transiently in blood donors with no known exposure to or history of hepatitis. Antibodies to hepatitis-associated antigen have been found in very few patients with acute or chronic hepatitis but occur commonly in hemophiliacs. The danger of transfusing blood containing antibody to hepatitis-associated antigen is not known.

Testing Methods

The most commonly used methods of testing for (immunodiffusion) hepatitis-associated antigen are agar gel diffusion and counterelectrophoresis (immunoelectroosmophoresis). Complement fixation, hemagglutination inhibition and radioimmunoassay are performed in certain research laboratories, but the National Academy of Sciences has recommended that they not be adopted for routine use at present.[26] The relative sensitivity of these methods when comparing titers is agar gel diffusion 1, agar gel diffusion using concentrated serum 5, counterelectrophoresis 5-15, complement fixation 100-

200, hemagglutination inhibition 100-200, and radioimmunoassay 100-200.[16] These figures can be misleading; however as they refer to *titers,* and comparable increases in patient or blood donor positivity are not found. For instance, Thulstrup[27] showed that in 32 patients with serum hepatitis, counterelectrophoresis increased the number of positive specimens 31% over agar gel diffusion, however, the number of patients with a positive test was increased only 3%. Gocke[18] found that counterelectrophoresis increased the number of hepatitis-associated antigen positive blood donors only to 18/3855 as compared with 17/3855 detected by agar gel difussion. Prince[25] found very little increased patient yield of hepatitis-associated antigen in cases of acute and chronic liver disease using counterelectrophoresis compared with agar del diffusion.

Experience in Minnesota

Since early 1970 investigation of hepatitis-associated antigen and blood donor testing has been performed in some Minnesota centers, notably Minneapolis War Memorial Blood Bank, University Hospital and the Mayo Clinic. Most of the testing was performed by agar gel diffusion using as antisera raw plasma or serum obtained from persons (usually hemophiliacs) who had the antibody to hepatitis-associated antigen. In January 1971 a standard antiserum was made available to all state health departments so that hepatitis-associated antigen testing of blood donors could be encouraged. Through the joint efforts of the Minnesota Department of Health, the Minnesota Medical Association (Committee on Blood and Blood Banks) and the Minnesota Association of Blood Banks, this antiserum was distributed to large blood centers in the state for routine testing of donors. Since that time, commercial reagents have been licensed for sale. Thus, contrary to one report,[28] Minnesota blood banks have been involved in hepatitis-associated antigen testing for quite some time and expanded this testing quickly and effectively when reagents became available.

The incidence of hepatitis-associated antigen positive blood donors in Minnesota is now well established and is quite low (Table 2). At this writing, all blood collected by Minneapolis War Memorial Blood Bank, St. Paul Regional Red Cross, Mayo Clinic and University of Minnesota is tested for hepatitis-associated antigen. Physicians should be aware that some centers use the agar gel diffusion method which requires 24 hours for hepatitis-associated antigen testing, thus testing of fresh products such as fresh whole blood or platelets may not be completed prior to transfusion.

TABLE 2

Results of Hepatitis-Associated Antigen Testing of Blood Donors from Different Centers Using Agar Gel Diffusion (AGD) and Counterelectrophoresis (CEP) Methods

Blood Donors	Test Method	Number Tested*	Number Positive	Percent Positive
University of Minnesota	AGD	11,138	11	.098
St. Paul Red Cross	AGD	27,020	9	.033
	CEP	36,417	13	.036
Minneapolis War Memorial Blood Bank	AGD	45,000	28	.06
Mayo Clinic+	AGD	8,816	5	.057
Boston+	AGD	1,800	4	.22
Denver+	AGD	600	4	.66
Chicago+	AGD	611	9	1.47

*Number represents specimens not individuals.
+Data from Taswell et al.[29]

Conclusions

Hepatitis-associated antigen testing is a valuable addition to pretransfusion testing of blood, but the test has significant limitations. Therefore, efforts to reduce transfusion-associated hepatitis should include not only hepatitis-associated antigen testing but also continued emphasis on thorough evaluation of the blood donor's medical history and the use of blood collected from volunteers. The most important step to decrease the hepatitis risk is judicious use of blood and blood components.

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See page 74 for references 6-28.

Classified Advertising

(Continued from page 50)

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INDICATIONS: Phenoxymethyl penicillin is indicated in the treatment of mild to moderately severe infections caused by penicillin G-sensitive microorganisms that are sensitive to the low serum levels common to this particular dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and by clinical response. Culture and sensitivity testing are especially important in suspected staphylococcal infections because increased resistance has been reported. Phenoxymethyl penicillin is not active against penicillinase-producing bacteria.

Note: Severe pneumonia, empyema, bacteremia, pericarditis, meningitis, and arthritis should not be treated with phenoxymethyl penicillin during the acute stage.

Indicated surgical procedures should be performed.

Medical conditions in which oral penicillin therapy is indicated as prophylaxis: For the prevention of recurrence following rheumatic fever and/or chorea. To prevent bacterial endocarditis in patients with congenital and/or rheumatic heart lesions who are to undergo dental procedures or minor upper respiratory tract surgery or instrumentation.

Note: Oral penicillin should not be used as adjunctive prophylaxis for genitourinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and childbirth.

CONTRAINDICATION: A previous hypersensitivity reaction to any penicillin.

WARNINGS: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. While more frequent following parenteral therapy, anaphylaxis has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

Some individuals with a history of penicillin hypersensitivity reactions have experienced severe hypersensitivity reactions from a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents, e.g., pressor amines, antihistamines and corticosteroids.

PRECAUTIONS: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

The oral route of administration should not be relied on in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility.

Occasional patients will not absorb therapeutic amounts of orally administered penicillin.

In streptococcal infections, therapy must be sufficient to eliminate the organism (10 days minimum); otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following completion of treatment to determine whether streptococci have been eradicated.

Prolonged use of antibiotics may promote the overgrowth of nonsusceptible organisms, including fungi. Should superinfection occur, appropriate measures should be taken.

ADVERSE REACTIONS: While the incidence of reactions to oral penicillins is much less than with parenteral therapy, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been reported with oral penicillin.

The most common reactions to oral penicillin are nausea, vomiting, epigastric distress, diarrhea, and black hairy tongue. The hypersensitivity reactions reported are skin eruptions (maculopapular to exfoliative dermatitis), urticaria and other serum sickness reactions, laryngeal edema, and anaphylaxis. Fever and eosinophilia may frequently be the only reaction observed. Hemolytic anemia, leucopenia, thrombocytopenia, neuropathy, and nephropathy are infrequent reactions and are usually associated with high doses of parenteral penicillin.

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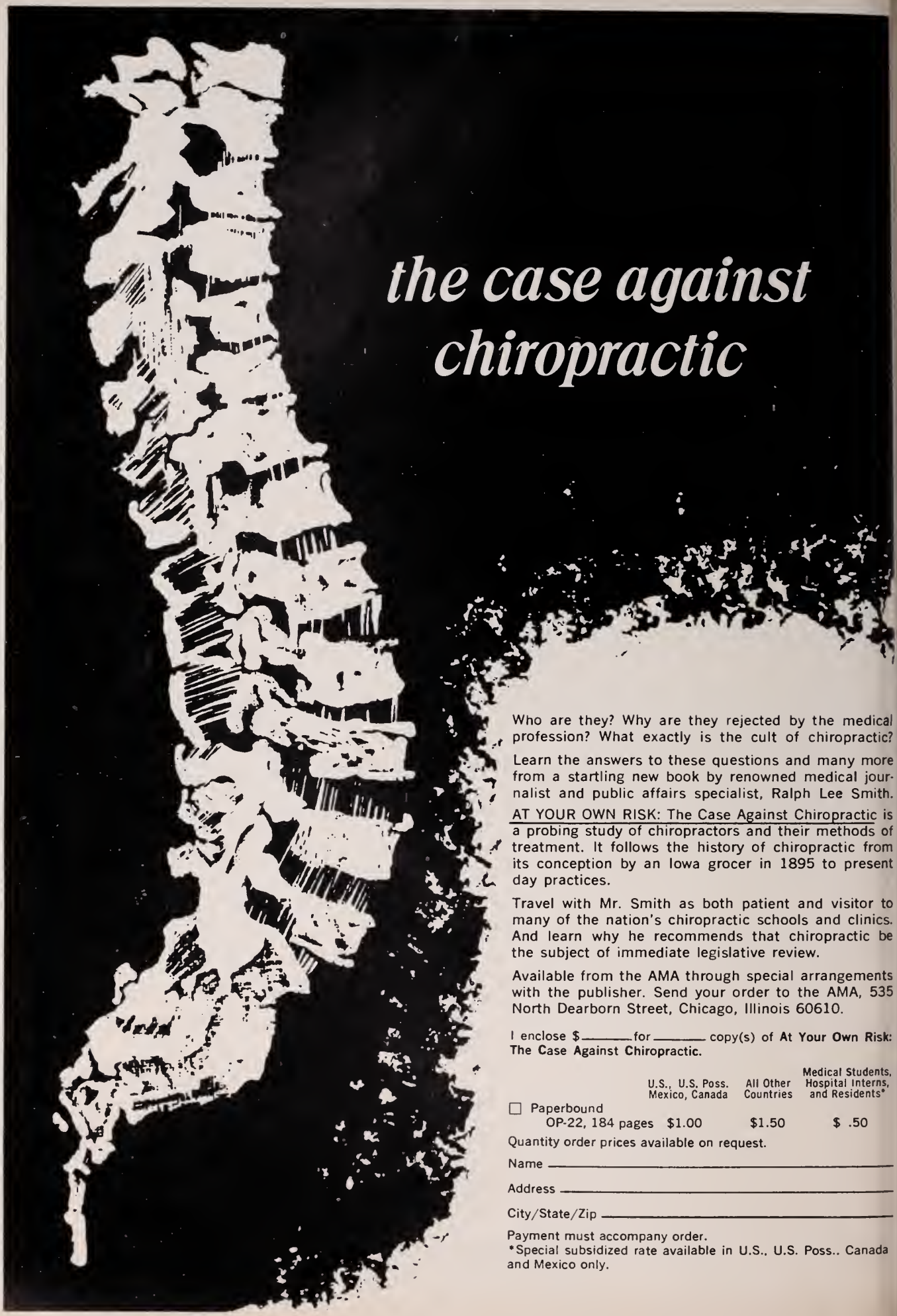
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Observing Externship for Sophomore Medical Students

LAUREL LEBENS;* LANCE PETERSON;* KEN SANSOME* AND JOHN VERBY, M.D.†

To SUPPLEMENT the basic science curriculum of the first two years of medical education with an introduction to clinical experience, students and staff at the University of Minnesota Medical School initiated an "observing externship" program for the class of 1972. Students (during their non-class hours) were placed with practicing physicians who volunteered their services in a mutual-learning experience. Students participated in the actual practice of medicine and learned basic clinical procedures; physicians were updated about medical education as it is. Both groups expressed satisfaction with the program and hope this experience will stimulate student consideration of a career in the practice of family medicine.

Traditionally medical education has been a two-year experience in the basic sciences based largely on didactic lectures and laboratory work followed by two-years' experience in clinical medicine. Since the 1972 class at the University of Minnesota was to be the last group to be so taught, some departments of the Medical School were willing to try new teaching approaches with this class.

In the spring of 1969, a discussion was held with the freshman class regarding the role of the general practitioner in dealing with psychiatric problems. An outline of newly planned programs for the incoming freshmen was also presented, which in turn interested members of the 1972 class.

As a result of this interest a program was arranged which permitted one or two students to meet with a practitioner every three or four weeks for a period of three to four hours. It was planned that one out of every four would be in a hospital visit with the remainder of the visits in the physician's office.

*Sophomore Medical Students, University of Minnesota Hospitals, Minneapolis, Minnesota.
†Associate Professor, Department of Family Practice and Community Health, University of Minnesota Hospitals, Minneapolis, Minnesota.

During the summer thirty physicians from the Twin Cities were contacted and volunteered for the program with the expectancy that thirty or forty students would like to participate. An orientation was held for the physicians, and the program goals were established: These were:

(1) To give students the opportunity to see the patient as a total person; (2) To allow the student to observe continuing comprehensive care of the patient and his family; (3) To give students the opportunity to see as much variety as possible from very simple to complex cases and (4) To allow the student to perform, under supervision, certain clinical skills such as knee aspirations, lumbar punctures, cut downs, IV starts, and normal deliveries. Physicians were asked to reduce patient load during student visits and to allow ample time for discussion of cases. The program was presented to students, for extracurricular involvement, in late September, and out of a class of approximately 150, 99 students desired to participate. By mid-November the program was under way with 99 students and 54 physicians.

Results

Student evaluation was sought at the completion of Fall and Winter quarters, the results of which appear in the following tables:

TABLE 1[1]

Comparison of Fall and Winter Questionnaire Responses from Sophomores Participating in the Observing Externship (N-99)

	Fall	Winter
% of students responding	83%	73%
% of students not meeting with assigned physician	5%	18%
Median number of sessions with physician	2	3
Median length of visit	2-5 hours	3-4 hours
Median number of patients per visit	5-10	6-10
Median number of hospital visits	1	1
Ratio of favorable:unfavorable comments on the program	11:1	8:1

TABLE 2[1]

*Sophomore Interest in Family Practice or General Practice After Two Quarters of the Observing Externship.**

Percent of Students Responding (N=60)

Very Interested	Mildly Interested	Undecided	Not Interested
60	28	12	0

*Taken from the Sophomore Observing Externship Questionnaire, Spring 1969.

Students began participating in physical diagnosis during the winter quarter as a scheduled part of the curriculum. This scheduled patient exposure may explain the small increase in lack of interest after winter quarter as shown in Table 1.

Stated criticisms of the program were: (1) Lack of student time; (2) Insufficient involvement in doing procedures; (3) Too many common, simple problems such as URI and (4) Lack of enthusiasm by some doctors.

Interest in family practice is shown in Table 2. Forty-five percent of those responding indicated the observing externship had affected their interest. Only three (5%) said they were less interested after participation.

Physician evaluation was sought at the end of spring quarter with a 63% return of questionnaires.

The overall response by physicians was favorable. They indicated a median number of 10 visits throughout the nine-month academic year to be an optimal arrangement. Of those responding, 80% felt the program was of benefit to the students.

A random sample of students not participating in the program, gave as reasons for not doing so: "not enough time" for outside activities while in medical school; a lack of communication with the physician and declining interest on the part of the student due primarily to required participation in the Physical Diagnosis Course during the spring quarter.

TABLE 3[1]

Responses of Participating Physicians Regarding Some Aspects of the Sophomore Observing Externship (N=34)

	Percent of Physicians Responding
Desire to continue as preceptor	91%
Prefer 1:1 rather than 2:1 student-physician ratio	75%
Willing to have student do more as opposed to being primarily observers	
(a) in the office	60%
(b) in the hospital	50%
Willing to work with Freshmen	67%

Conclusion

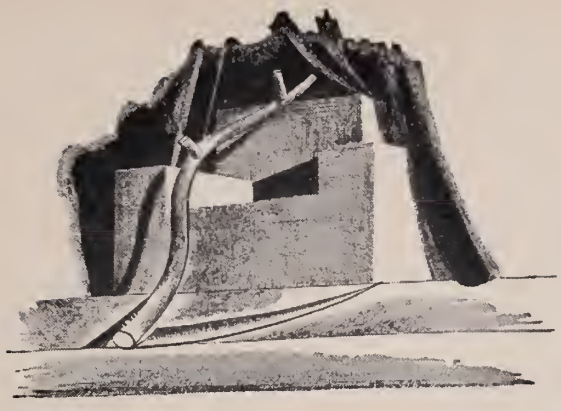
From analysis of student evaluation data, the envisioned "Observing Externship Program" was a worthwhile experience for those students participating with a physician who was interested in teaching and achieving the goals of the program. The vast majority of physicians fulfilled the students' expectations. Since the basic criticism of the program was not enough extracurricular time available, this program should be made an integral part of the medical curriculum.

Reference

1. Cassie, Josephine M.: "A Look at the Undergraduate Programs of the Department of Family Practice and Community Health." A Report to the Educational Policy Committee, University of Minnesota, July 21, 1970.

Our Congratulations

Dr. Frank Hammond Krusen became the first honorary member of the Minnesota Physiatric Socicty on November 21, 1970. He had been nominated for this honor on September 15, 1970. An illuminated scroll, recognizing "his many contributions to the practice and advancement of physical medicine and rehabilitation," was presented in absentia at the time of the scientific meeting of the Society.



In Memoriam

A great man who neither sought nor shunned greatness, who found glory only because glory lay in the plain path of duty.—Macaulay

EDWARD J. ENGBERG, M.D.

Dr. Edward J. Engberg, 83, former superintendent of the Faribault State School and Hospital, died July 18. Born in Minneapolis, he was a graduate of the University of Minnesota Medical School. Dr. Engberg was a specialist in neuropsychiatry.

He was a member of the Phi Rho Sigma Medical Fraternity, a life member of the American Psychiatric Society, past president of the American Association on Mental Deficiency, a member of the Southern Minnesota Medical Society, diplomate of the Board of Psychiatry and Neurology, member of the Rice County Medical Society and American Medical Association, and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Engberg is survived by his son and daughter.

ALVAN SACH-ROWITZ, M.D.

Dr. Alvan Sach-Rowitz, 77, Moose Lake physician and surgeon, died July 31. He was a graduate of St. Louis University Medical School and had practiced in Moose Lake since 1932.

He was a medical staff member of the Moose Lake Community Hospital and Mercy Hospital, a member of the St. Louis County Medical Society and the American Medical Association and a 50 Club Member of the Minnesota State Medical Association.

Dr. Sach-Rowitz is survived by his wife.

WILLIAM CARL KAUFMAN, M.D.

Dr. William C. Kaufman, 89, one of Minnesota's oldest practicing physicians, died May 8. On September 1st of last year, he would have completed 60 years of service to Appleton.

He had been mayor of Appleton several years, a member of the Board of Education for 11 years, president of the Kandiyohi-Swift-Meeker County Medical Society and the Camp Relief District Medical Society. Dr. Kaufman was a member of the American Medical Association, a surgeon for both the Milwaukee and Great Northern Railways and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife, daughter, and a son, Dr. William C. Kaufman II of Green Bay, Wisconsin.

BERNARD SPENCER NAUTH, M.D.

Dr. Bernard S. Nauth, 60, general practitioner, died June 4. Born in Minneiska, Minnesota, Dr. Nauth attended the University of Minnesota Medical School. He had practiced in Winona, Minneapolis and Arizona.

He was a member of the Ramsey County Medical Society, American Medical Association and the Minnesota State Medical Association.

Dr. Nauth is survived by his wife and four children.

EMMETT V. KENEFICK, M.D.

Dr. Emmett V. Kenefick, 72, St. Paul physician, died June 24. Dr. Kenefick was born in Belmond, Iowa, and attended the University of Iowa Medical School.

Dr. Kenefick was vice president-elect of the Minnesota Academy of Medicine, a member of the Minnesota Society of Internal Medicine, Minnesota Academy of Medicine, Sigma Chi, Alpha Omega Alpha, Ramsey County Medical Society, American Medical Association and a Life Member of the Minnesota State Medical Asociation.

He is survived by his wife, daughter, and three sons.

RICHARD O. BURMEISTER, M.D.

Dr. Richard O. Burmeister, 52, St. Paul anesthesiologist, died July 21. Born in St. Paul, Dr. Burmeister attended the University of Minnesota Medical School.

He was former Chief of Staff at Midway Hospital and a member of the Ramsey County Medical Society, the Minnesota State Medical Association and the American Medical Association.

Dr. Burmeister is survived by his wife, six daughters and one son.

CLAUDE J. EHRENBERG, M.D.

Dr. Claude J. Ehrenberg, 77, of Boca Raton, Florida, retired Chief of Staff at Northwestern Hospital, died June 16. A Minneapolis native and former professor of obstetrics and gynecology at the University of Minnesota, Dr. Ehrenberg was a former medical director of the Hennepin County League for Planned Parenthood.

A former president of the Hennepin County Medical Society, he was also a member of the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Ehrenberg is survived by his wife, three sons and a daughter.

HERMAN O. McPHEETERS, M.D.

Dr. H. O. McPheeters, retired Minneapolis surgeon and a pioneer in the treatment of varicose veins, died July 20. He was 80. A native of Mankato, he graduated from Northwestern University Medical School and practiced in Genoa, Illinois, and Redwood Falls, Minnesota, before going into practice in Minneapolis.

He was a member of the American Medical Association and the Hennepin County Medical Association, and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. McPheeters is survived by his wife, a daughter and a son.

RALPH D. HANOVER, M.D.

Dr. Ralph Hanover, 64, International Falls physician, died June 13. His medical education was obtained at the University of Minnesota Medical School.

He was a member of the Range Medical Society, the American Medical Association, Academy of General Practice, the Industrial Medical Association, and the Minnesota State Medical Association.

Dr. Hanover is survived by his wife, a son and a daughter.

THORVOLD J. JENSEN, M.D.

Dr. T. J. Jensen, 89, general practitioner and surgeon in Duluth for more than 60 years before his retirement, died March 8. Born in Bergen, Norway, Dr. Jensen came to the United States as an infant. He was graduated from Hamline University Medical School.

Dr. Jensen was a member of the St. Louis County Medical Society, American Medical Association and an honorary member of the St. Luke's and St. Mary's hospitals' staffs and a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his two daughters and two sons.

PETER ARNOLD LOMMEN, M.D.

Dr. Peter A. Lommen, 77, longtime Austin physician, died March 16. A native of Vermillion, South Dakota, Dr. Lommen graduated from Rush Medical School in Chicago. He came to Austin in 1920 and had been a member of the St. Olaf Hospital staff since its organization.

Dr. Lommen was a member of the Mower County Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife and four sons, two of whom practice medicine in Austin.

CHARLES L. LICK, M.D.

Dr. Charles L. Lick, 78, St. Paul physician, died March 27. Born in St. Paul, he was a lifelong resident of the city and a physician and surgeon in St. Paul for more than 50 years.

He was a member of the Ramsey County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Lick loved to play golf and keep abreast with all the latest concepts of medicine and surgery. He was very proud of a case history of a young woman with a giant cell tumor and enjoyed telling this story.

Dr. Lick is survived by his widow and a son, Dr. Louis C. Lick of Edina.

KNUTE A. SPORRE, M.D.

Dr. Knute A. Sporre, 78, Fergus Falls physician, died March 17. In his early adolescence, Dr. Sporre had come to the United States from Sweden and later graduated from the University of Iowa College of Medicine in 1919. In his early practice, he had served southwestern Minnesota and northwestern Iowa.

Dr. Sporre was a member of the Park Region District and County Medical Society, the American Medical Association and was a 50 Club and member of the Minnesota State Medical Association.

GEORGE E. NELSON, M.D.

Dr. George E. Nelson, 46, Minneapolis orthopaedics surgeon, died September 28. Born in Detroit, Michigan, Dr. Nelson later attended the University of Minnesota Medical School.

He was a member of the Hennepin County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Nelson is survived by his wife, a son, and two daughters.

KENNETH W. WILDER, M.D.

Dr. Kenneth W. Wilder, 87, Minneapolis physician, died October 8. He had practiced medicine in Minneapolis over fifty years and was Assistant Chief of Staff of St. Barnabas Hospital.

Born in Morristown, Minnesota, Dr. Wilder attended the University of Minnesota Medical School. He was a member of the Hennepin County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

HARRY LEROY BERGE, M.D.

Dr. Harry Berge, 53, Mora physician died September 9th of a heart attack while on a hunting trip. He had received his medical education from the University of Minnesota.

A member of the East Central County Medical Society and the American Medical Association, Dr. Berge was also a member of the Minnesota State Medical Association.

He is survived by his wife and two children.

JAMES H. MATTHEWS, M.D.

Dr. James Matthews, 46, professor of anesthesiology at the University of Minnesota and one of the leading nominees for the position of dean of the Medical School, died October 7, in Hartford, Connecticut, of an apparent heart attack. He was attending a meeting of the American Board of Anesthesiology and was president-elect of the organization.

He was a member of the Ramsey County Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Matthews is survived by his wife, a daughter and two sons.

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Clinical Path Conference

Abdominal Pain, Confusion, and Intermittent Fever in an Elderly Male

CALVIN L. STRAND, M.D.* and ROBERT A. VAN TASSEL, M.D.†

First Admission

A 73-year-old man, rather darkly pigmented and cachectic was admitted to the hospital because of abdominal pain. He was confused, disoriented and unable to give much history. He said that he had not eaten for five days and was too weak to walk.

Physical Examination

His blood pressure was 140/70; pulse 70 and regular; respirations 16; and temperature 99°. His mucous membranes were dry and his skin turgor poor. The lungs were clear. His heart was not enlarged. A moderately loud systolic murmur was heard at the left sternal border and transmitted into the right side of the neck. The abdomen was distended and physical signs of ascites were present. There was no abdominal tenderness, no palpable organs or masses. The remainder of the physical examination was normal.

Laboratory

Hemoglobin was 13.1 gm % on admission but fell to 10.7 gm % after overnight hydration. White blood count was 6,800 with 77% neutrophils, 24% lymphocytes and 1% monocytes. The urine had a specific gravity of 1.017, gave a 1+ test for albumin, but contained no sugar and no formed elements. Serum sodium was 146 mEq/L; potassium 3.4 mEq/L; chloride 97 mEq/L; CO_2 25 mEq/L. Total serum proteins were 6.7 gm % with 2.0 gm % albumin. Alkaline phosphatase was 15 KA units; bilirubin 1.9 mg % and blood urea nitrogen 15 mg %. Blood glucose was 129 mg %. A cephalin flocculation test was 4+ and thymol turbidity 18.5 units. The serum transaminase was 60 units. The prothrombin time was 13.6 seconds with a control of 12.6 seconds. An electrocardiogram revealed non-specific ST-T changes.

A chest roentgenogram was normal except for elevated diaphragms. Abdominal films showed evidence of ascites. An excretory urogram revealed small kidneys with slight loss of the renal cortices. The collecting systems appeared normal. A brain scan and an upper gastrointestinal series were normal. A liver scan reportedly showed a small liver.

Cultures of the sputum, urine, and stool produced no pathogenic organisms; smears of sputum for acid-fast bacilli were negative. Red cell indices were as follows: MCV: 89; MCH: 27; MCHC: 31.

Hospital Course

Throughout his hospital course the patient remained somewhat confused and withdrawn. On several days his temperature rose to between 101° and 102° but then returned to normal without specific therapy. On the second hospital day a diagnostic paracentesis was performed with removal of 500 cc of reddish-brown fluid containing 220 white blood cells 77% of which were mononuclear cells, 14% neutrophils and 9% tissue cells. The ascitic sugar content was 125 mg %; the protein 2.4 gm %, and the specific gravity 1.016. The fluid contained 16,250 red blood cells per cubic millimeter. Smears for acid-fast bacilli were negative. Cytological examination demonstrated "abundant red cells, numerous small mononuclear cells, lymphocytes and histiocytes." There were no malignant cells.

The serum iron determination was 40 mcg % with an iron-binding capacity of 139 mcg % and the resulting saturation of 29%. Serum vitamin B-12 was 1,625 picogram‡/ml. (normal 150 to 600 picograms/ml.) and folic acid 2.4 millimicrograms/ml. (normal 5.3 to 17). The patient was given a multiple vitamin preparation and supplemental thiamine as well as ferrous gluconate and folic acid. On the 25th hospital day he was discharged to a nursing home.

*Formerly Resident, Department of Pathology, Hennepin County General Hospital, Minneapolis, Minnesota. Presently, Chief of Laboratory Service, Memphis Naval Hospital, Millington, Tennessee.
†Former Resident, Department of Internal Medicine, Hennepin County General Hospital Minneapolis, Minnesota. Now practicing in Minneapolis.
‡One picogram = 10^{-12} grams.

Second Hospitalization

Approximately two weeks after discharge the patient developed a temperature of 103°, became unresponsive, and was re-admitted to the hospital. Examination: The patient was stuporous with only slight response to painful stimulation. The blood pressure was 60/40; pulse 120; temperature 102.2°. His skin was warm and dry with peripheral cyanosis. The conjunctiva of the right eye was reddened and the orbit was red and edematous; the pupils were of equal size and reacted normally to light. A purulent discharge was present in the right ear canal. The neck was rigid. The lungs were clear. The heart was of normal size. Occasional premature beats were audible but no murmur was heard. The abdomen was flat and sunken and no masses or organs were felt. There was a hematoma present over the right elbow and a superficial skin laceration near the right wrist. Deep tendon reflexes were hypoactive but symmetrical.

The hemoglobin was 10.5 gm %; the white blood count 8,400 with 88% neutrophils and 12% lymphocytes. Toxic granulations were described in the neutrophils. The urine was yellow with a specific gravity of 1.015 and gave a 2+ test for albumin and a negative test for sugar. Microscopic examination of the urine revealed packed fields of white blood cells. The cerebrospinal fluid was clear, contained no cells and had a protein content of 125 mg % and a sugar of 20 mg %. The blood glucose was 55 mg %. Serum sodium was 151 mEq/L; potassium 2.6 mEq/L; chloride 106 mEq/L; and CO_2 21 mEq/L. The blood urea nitrogen was 36 mg %. Specimens of cerebrospinal fluid, blood, urine and the discharge from the right ear were submitted for culture and treatment was begun with kanamycin and cephalothin.

Despite these antibiotics and the administration of intravenous fluids, the patient's blood pressure continued to fall and he expired four and one-half hours after admission.

Dr. Robert Van Tassel:

The case is that of a 73-year-old cachectic male with ascites. The history is of little help in arriving at a diagnosis and the laboratory is not particularly revealing. The differential diagnosis is that of a cachectic male with ascites, and would include cirrhosis, neoplasm with peritoneal implants, tuberculosis, hepatoma, congestive heart failure, pancreatitis and peritonitis. Let us now consider each of these major diagnostic possibilities with respect to this case.

Cirrhosis

The ascitic fluid in cirrhosis is classically a transudate: it has a low specific gravity, a low protein, and usually is clear yellow. The specific gravity is usually less than 1.008 and very rarely exceeds 1.015. The protein content is generally between 1 to 2 gm %, and only rarely exceeds 3 gm %. The ascitic fluid in this patient is bloody, with many mononuclear cells, and an elevated protein; it is not the classic ascitic fluid seen in cirrhosis. However, one may occasionally see serosanguineous ascitic fluid in cirrhotic patients. When present it is thought to be a result of a breakdown of adhesions about the liver as it contracts in size. Thus the ascitic fluid could be secondary to cirrhosis, although the content of the ascitic fluid produced in this case was not entirely typical.

Neoplasms with Peritoneal Implants

A serosanguineous fluid, high in protein content, is characteristic of the ascitic fluid associated with carcinomatosis. An experienced cytologist will find malignant cells in the ascitic fluid in 50 to 60% of the cases. No mention is made of positive cytology on the examination of the ascitic fluid in this case. The primary site for carcinoma with metastasis to the peritoneum would be stomach, pancreas, colon or rectum. In the female, the ovary would be added to this list. Primary carcinoma of the peritoneum is a very rare disease and is not usually associated with ascites. Rapid emaciation and cachexia are the rule. The serosanguineous ascitic fluid strongly suggests malignancy.

Tuberculosis

Tuberculous peritonitis or miliary tuberculosis with ascitic fluid production is found most commonly in children. Patients with ascites secondary to tuberculosis almost without exception have some manifestation of tuberculosis elsewhere in the body. The fluid may be serosanguineous and has many mononuclear cells. The characteristic features are abdominal pain, fever, and evidence of tuberculosis elsewhere. The liver function studies are usually normal. Occasionally one can feel the thickened nodules in the peritoneum on examination of the abdomen. In this case, the ascitic fluid is certainly consistent with a diagnosis of tuberculosis. However, the absence of evidence of tuberculosis on the chest x-ray or elsewhere in the body, and the fact that the acid-fast stain of the peritoneal fluid was negative would tend to make this diagnosis less likely.

Hepatoma

Ascites is present with hepatoma in approximately 60 to 70% of the patients. The fluid is characteristically serosanguineous. The liver is hard and enlarged in three of four cases. The classic laboratory finding is a high alkaline phosphatese with a moderately elevated serum bilirubin. Hepatoma is more common in men and most common in the fifth and sixth decades. It is associated with cirrhosis and is 20 times more frequent among cirrhotics than among the general population. The findings of the laboratory analysis of the ascitic fluid in this case would be consistent with, although not diagnostic of, a hepatoma. The fact that the patient's liver was not palpable and that the liver scan showed a small liver would make the diagnosis of hepatoma unlikely.

Congestive Heart Failure

Classically, patients with congestive heart failure may have ascites; however, the absence of other manifestations of congestive heart failure and the normal chest x-ray make a diagnosis of congestive heart failure quite unlikely. Constrictive pericarditis would have to be considered, but the other characteristic findings of constrictive pericarditis are not given in the protocol; therefore this would be an unlikely diagnosis.

Hemorrhagic Pancreatitis

Hemorrhagic pancreatitis commonly produces ascites. The ascitic fluid is serosanguineous and would be compatible with fluid obtained in this case. Nevertheless, the history is not consistent with that of hemorrhagic pancreatitis and the physical examination of the initial admission showed no evidence of abdominal pain or tenderness. No mention is made of an elevated amylase in the serum, urine or ascitic fluid. The diagnosis of hemorrhagic pancreatitis, I believe, can be excluded.

Peritonitis

Peritoneal irritation secondary to bacterial invasion usually produces an acute abdomen with prominent findings. Serosanguineous ascitic fluid can be produced but it is not common. The finding of many mononuclear cells in the ascitic fluid and the physical examination in this case helps rule out this diagnosis.

Additional Data

Normochromic Anemia

A normochromic, normocytic anemia which is non-diagnostic but is compatible with most of the entities was being considered.

Vitamin B-12

The serum B-12 level is 1,640 picograms/ml, which is markedly elevated. The B-12 levels are markedly elevated in acute myeloblastic leukemia, chronic myelocytic leukemia, and chronic liver disease. However, it is possible this patient had a serum level drawn shortly after the administration of intramuscular B-12; so it is doubtful that the elevated B-12 would be of help in arriving at the diagnosis in this case.

Folic Acid

The serum folic acid is 2.4 millimicrograms/ml, which is slightly below normal and consistent with a 74-year-old cachectic male with liver disease. This probably represents dietary deficiency.

Serum Iron

Serum iron is 40 mcg % and iron-binding capacity is 130 with 29% saturation; both are consistent with chronic infection. Anemia is found in 75% of cases of chronic liver disease and is usually associated with blood loss, increased hemolysis or decreased erythropoiesis as well as with vitamin deficiency.

Liver Function Tests

The liver function studies are compatible with those of a long-standing cirrhotic. The bilirubin is mildly elevated to 1.9 mg % and the alkaline phosphatese is 15 KA units; the cephalin floc is 4+; the thymol turbidity, 18.5; the SGOT, 60 units; and the prothrombin time is 13.6 with a control of 12.6. The 4+ cephalin flocculation and the thymol turbidity of 18.5 would both indicate fairly long-standing liver disease. All the liver function abnormalities could be explained on the basis of cirrhosis.

Progress

The patient's hospital course showed him to be intermittently confused and febrile, but confusion in the elderly hospitalized male is not at all uncommon. Nevertheless, one would have to consider hypoxia, chronic subdural hematoma, drug intoxication, cerebrovascular disease, or neurosyphilis. Intermittent fever is consistent with chronic liver disease, occult malignancy, and bacterial infections such as tuberculosis and fungal disease. Specimens of blood, urine, and sputum from this patient apparently were cultured for pathogenic organisms and none were found. Therefore, organisms that are not as readily cultured such as Mycobacterium tuberculosis must be strongly considered.

The patient was discharged from the hospital to a nursing home and was re-admitted in septic shock two weeks later. His blood pressure was 60/40, his temperature was 104°; and he was unresponsive. At this time the physical findings of a "red orbit and red conjunctiva" along with a draining right ear make the diagnosis of cavernous sinus thrombosis very tempting. However,

no supporting evidence for cavernous sinus thrombosis is present, such as pupillary changes which may or may not be present, involvement of cranial nerves II, III, IV, and VI which travel through the cavernous foramen, edema of the eyelid or cornea, or papilledema. The cerebrospinal fluid is clear and has a normal pressure which makes the diagnosis of cavernous sinus thrombosis untenable. The cerebrospinal fluid protein was elevated to 125 mg % and the sugar reduced to 20 mg %. The low cerebrospinal fluid sugar is probably a reflection of a low blood glucose level of only 55 mg %. The elevated spinal fluid protein, however, must be explained. Isolated cerebrospinal fluid protein elevation with a normal cell count is seen in myxedema, collagen disease, diabetes mellitus, and tumor. In this case there is no evidence of myxedema, collagen disease, or diabetes; however, the possibility of malignancy is a consideration. For instance, carcinoma of the pancreas with metastasis to the peritoneum and brain could result in the production of serosanguineous ascitic fluid and mental confusion, as seen in this case. But the absence of other findings suggestive of a tumor, including a negative ascitic fluid, discount this diagnosis. The final diagnosis would most likely be alcoholic liver disease as manifested by cirrhosis and supported by the small liver. The patient's demise was probably due to gram-negative septicemia which may have been from his urinary tract; also aspiration pneumonia cannot be entirely ruled out.

Pathology Discussion

Dr. Calvin Strand:

One factor which made this a difficult clinical diagnostic case was that this patient was suffering from multiple diseases.

Autopsy findings: The body was that of an elderly, cachectic white male. There were approximately three to four liters of brown fluid in the peritoneal cavity. The peritoneal surfaces displayed numerous adhesions but no evidence of tumor. The heart was of normal weight (300 gm), but the right coronary artery showed marked atherosclerotic narrowing at its take-off with only a pin-point lumen remaining. Also the left coronary artery revealed significant narrowing, particularly in its terminal branches. Microscopic examination of the myocardium showed diffuse patchy fibrosis but no evidence of acute infarction. The lungs were relatively heavy with a combined weight of 1950 gm. At the time of the gross autopsy it was stated that the lungs appeared somewhat consolidated and pneumonia was suspected. However, when the histologic sections were examined later, an interesting and extremely important finding was present. The pulmonary parenchyma was studded with numerous granulomas, most of which showed central caseation (Figure 1). A Ziehl-Neelsen stain revealed the presence of slender straight acid-fast bacilli. The fact that the granulomas were quite small and studded throughout all of the lung blocks taken at autopsy suggested a miliary pattern of distribution. The liver was rather small, weighting 1,000 gm. The external surface was reddish-yellow in color and somewhat nodular, suggesting cirrhosis. The histologic sections showed general loss of the normal lobular architecture and the presence of numerous large connective tissue bands connecting adjacent portal areas. The latter features are consistent with Laennec's cirrhosis. Also, numerous granulomas were scattered throughout the hepatic parenchyma (Figure 2), some of which again showed central caseation. The liver also displayed the findings of alcoholic hepatitis (Figure 3). as represented by the presence of numerous cytoplasmic, eosinophilic masses

having the appearance of alcoholic hyaline, fatty metamorphosis, focal areas of hepatocellular degeneration, and a polymorphonuclear leucocytic infiltrate. The spleen showed involvement with numerous granulomas. One of the adrenal glands also contained a small granuloma made up of epithelioid cells and inflammatory cells. Histologic examination of the peritoneal surfaces showed no evidence of tuberculosis. The brain and kidneys revealed no evidence of involvement, either. Unfortunately, the bone marrow was not examined.

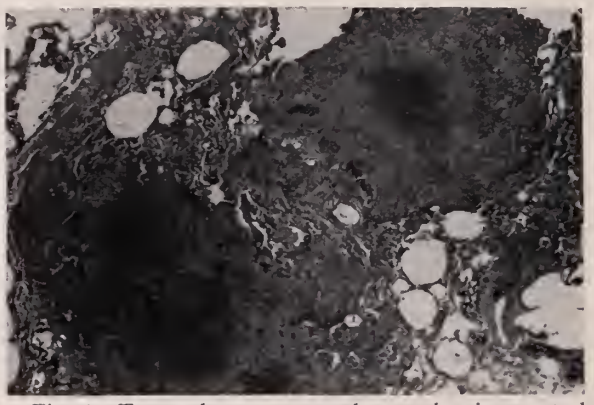


Fig. 1—Two pulmonary granulomas showing central caseation necrosis.

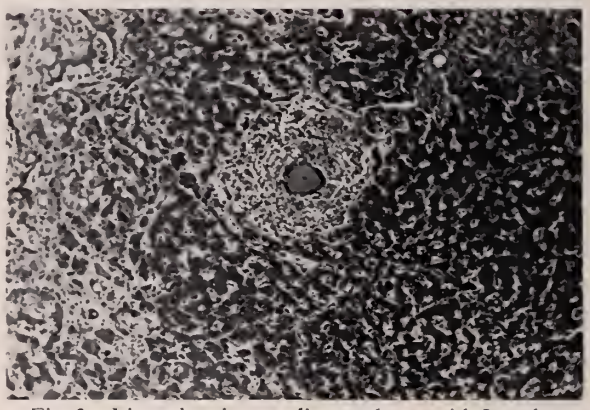


Fig. 2—Liver showing small granuloma with Langhans-type giant cell in center.

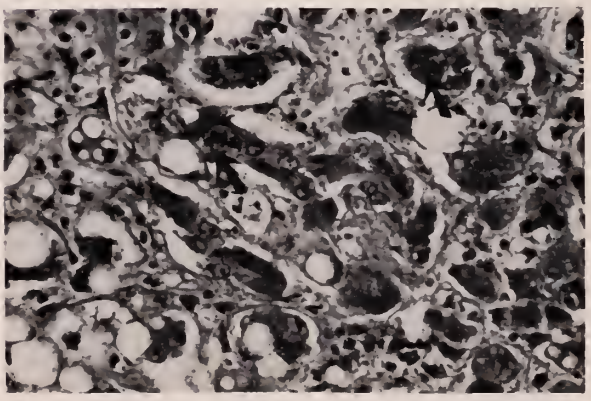


Fig. 3—Liver showing features of alcoholic hepatitis including alcoholic hyaline (arrows).

Pathologic Diagnoses

1. Miliary tuberculosis involving the lungs, liver, spleen, and adrenals.
2. Laennec's cirrhosis and acute alcoholic hepatitis.
3. Marked coronary artery atherosclerosis with diffuse myocardial fibrosis.

Miliary tuberculosis refers to that form of tuberculosis produced by dissemination of the tubercle bacilli throughout the body through the blood stream and characterized by the development of innumerable small tubercles in certain organs which are most susceptible to the infection. Tubercle bacilli may get into the blood stream either by the lymph vessels and lymph nodes, or by the rupture of a caseous focus into a blood vessel. Certain organs such as the lungs, liver, spleen, adrenals, kidneys and meninges seem to be most susceptible to miliary infection. This disease is most apt to occur at the extremes of life, and adrenal steroid therapy and pregnancy increase susceptibility.

The clinical picture is quite variable. The patient may be acutely ill with night sweats, chills, fever, cough and weight loss; and the disease may progress rapidly, causing death before a diagnosis can be established. At other times, the disease may be insidious with little fever and only weakness and weight loss. The physical examination is usually non-contributory except that one may observe tubercles in the optic fundi on funduscopic examination. A chest film may be helpful in showing numerous tubercles. However, it must be remembered that a complete clinical picture may precede development of the x-ray picture. The tuberculin test may be negative (anergic) in an acutely ill patient. It is extremely important to make the diagnosis, however, as untreated miliary tuberculosis is invariably fatal and is frequently complicated by the development of tuberculous meningitis. It is worthwhile to remember that miliary tuberculosis often involves the retina, bone marrow, and liver, and that these sites offer valuable clinical opportunities to make the diagnosis. The tubercles can be visualized in many instances in the eyegrounds by simple funduscopic examination; and bone marrow aspiration and liver biopsy provide the opportunity for identifying, by both cultural and histologic techniques, the miliary dissemination of the organism.

Cases of undiagnosed fatal tuberculosis, such as the one discussed today, are not as uncommon as one might suspect. Casey,[1] reporting on 2,000 autopsies done in a five-year period, states that tuberculosis was the main cause of death in 28 or 1.4% of the cases. Interestingly enough, tuberculosis was undiagnosed in 14 of these cases (0.7%) and was not recognized at the gross postmortem in seven cases (0.35%). Thus, this is a disease that may be missed not only clinically but also at gross autopsy and not recognized until the time of microscopic examination of the autopsy tissue sections.

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Some people never exaggerate. They just remember big.

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Legislative

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What's It All About??

R. L. ENGWALL, M.D.*

TEN YEARS AGO the AMA is frank to say, the medical profession had difficulty getting members of Congress to listen to its views. This is not the case today according to AMA's representatives in Washington. This noticeable change, most observers feel, can be credited to the medical PAC movement. Money raised and distributed by AMPAC (American Medical Association Political Action Committee), the AMA's political arm and its state counterparts, such as MINNPAC (Minnesota Medical Political Action Committee), has in fact created a considerably better climate in which medicine's views are heard on the multitude of health related legislation continually facing the Congress.

This improved legislative climate is a direct result of increasing and focusing physician involvement in the election process through a single organization. Greater impact is thus provided in helping to elect responsible men and women in both parties to Congress and to our own Minnesota State Legislature.

AMPAC was formed in 1961 to provide AMA members with a legal vehicle for direct contribution to political candidates. MINNPAC (formerly NUHOPE) was established in 1962 as the State counterpart to AMPAC.

The Federal Corrupt Practices Act forbids political contributions by tax exempt organizations such as the AMA and Minnesota State Medical Association. Like the COPE, the AFL-CIO's Committee on Political Action, AMPAC/MINNPAC solicits individual contributions to support political candidiates. In Minnesota each $25.00 contributed provides the physician, physician's wife or other contributor with a $15.00 MINNPAC membership and a $10.00 AMPAC membership. Also available and encouraged are sustaining memberships of $100.00 which are divided equally between AMPAC and MINNPAC.

MINNPAC and AMPAC have two basic objectives. The first is to provide political education for physicians and their wives to encourage them to participate actively in politics. The second is to provide direct assistance to candidiates for political office by mobilizing volunteers and financial contributions.

MINPAC dues dollars are used primarily to help elect State legislators in both parties who will maintain a responsible, open minded attitude towards health related legislation.

AMPAC dues dollars are used similarly in Congressional races throughout the country including Minnesota. For every dollar that AMPAC contributes, however, it is estimated that four or five times that much is raised additionally by state and local candidate support committees which have been organized.

AMPAC and its state and local counterparts (MINNPAC) rank very high among political organizations in terms of the money they disburse to political candidates—perhaps second only to COPE. An unidentified member of Congress has been quoted as saying, "If it hadn't been for AMPAC, a good many members of Congress would not be here today." The impact of this medical political action has strengthened medicine's voice in the Congress and in the state legislature.

AMPAC and MINNPAC do not lobby; this is a function of the AMA and the Minnesota State Medical Association. PAC activities, however, have been a great assistance to the legislative efforts of both the AMA and Minnesota State Medical Association. Former AMA President, Walter C. Bornemier, expressed it this way: "Before AMPAC was formed 10 years ago, we couldn't even get an audience with Congressmen or legislators. Now, we are heard and respected. AMPAC has helped us buy the right to a dialogue."

Dr. John L. Falls, Chairman of the Minnesota State Medical Association Committee on Public Policy states that there is no question but that Minnesota State Medical Association representatives are given a better hearing by State legislators who have had physician support through MINNPAC in their own districts at campaign time. He feels emphatically that MINNPAC has been of great assistance to the Minnesota State Medical Association in accomplishing its legislative goals and objectives.

AMPAC and MINNPAC are both non-profit,

*Chairman, Minnesota Medical Political Action Committee.

unincorporated bodies. AMPAC's activities are supervised by a bi-partisan ten-man Board of Directors appointed annually by the AMA's Board of Trustees. MINNPAC has a Board of Directors consisting of nine Councilor District representatives appointed by the Minnesota State Medical Association Council plus two directors from each of Minnesota's eight Congressional Districts and from three to five more additional at large directors selected by the 9 Councilor District representatives.

A candidiate review committee appointed by these directors makes recommendations to the MINNPAC Board of candidates who they feel merit financial support based on the candidates voting record and/or his receptivity to medically related issues. The opinions of physicians in the candidate's district is also solicited in making these evaluations on candidate support.

In 1970 MINNPAC contributed financially to 108 State Senate and House candidates out of a possible 202 contests. Eighty-eight percent of the DFL candidates and 65% of the conservative candidates, were winners.

Nationally AMPAC was successful in over 75% of the Congressional campaigns it participated in.

While the track record of AMPAC and MINNPAC is good, it can and must be improved on. Many physicians have yet to write their first $25.00 check to MINNPAC. The impact of MINNPAC and AMPAC would be increased considerably were all Minnesota physicians to become members in 1972.

Each year the volume of health related legislation grows in number and complexity at both the state and national levels. It is, therefore, imperative that medicine becomes more actively involved in the election of candidates who are knowledgeable and responsible in their attitude toward improving the delivery of health care. Active personal involvement in campaigns is most desirable, however, MINNPAC membership dues provide the physician and his wife an opportunity to help strengthen medicine's voice with but a small financial expenditure.

The 1972 elections will be crucial for medicine. Every physician who is concerned with the type of national health insurance which will presumably be enacted in 1973 should be vitally interested in helping to elect the right men and women to Congress in 1972, not only in Minnesota but all over the nation. New MINNPAC memberships are essential to fulfill this objective.

At the AMA meeting this summer, the President of the United States addressed the House of Delegates and challenged them with this statement: "America needs leadership from you in the medical profession, and your wives. I know many of you are so concerned whenever anybody suggests that you get into politics, and I do not speak in any partisan sense. I am not concerned whether you are in one party or the other. The main thing is to be in. I have heard a doctor say on occasion, 'I am only interested in my profession; I am not interested in politics.' Let me tell you something, he better get interested in politics or he won't have any profession to be interested in." In that statement, President Nixon said it all.

Was there no milder way but the smallpox,
The very filth'ness of Pandora's box?
So many spots, like *noeves*, our Venus soil?
One jewel set off with so many a foil!
Blisters with pride swell'd, which thro' 's flesh did sprout,
Like rose-buds, stuck i' th' lily skin about.
Each little pimple had a tear in it,
To wail the fault its rising did commit:
Who, rebel-like, with their own lord at strife.
Thus made an insurrection 'gainst his life.
Or were these gems sent to adorn his skin,
The cab'net of a richer soul within?
No comet need foretell his change drew on,
Whose corpse might seem a *constellation*.*

*John Dryden: Upon the Death of the Lord Hastings. Lines 53-66, 1649.



Book Reviews

HEREDITY, DISEASE & MAN: GENETICS IN MEDICINE by Alan E. H. Emery, M.D.; University of California Press, Berkeley and Los Angeles; 1968; Price: $6.85.

This book is the second volume in the series "Perspectives in Medicine" published by the University of California Press. The advances in genetics are coming so rapidly that the gap between the technical information reported in conferences and published in journals and that which is available to the general physicians or interested non-medical personnel has become increasingly wide.

This short and readable book presents the current fundamentals of genetics in terminology which is understandable by high school or college graduates working in fields related to medicine or who merely have the curiosity to know more about genetics. Because it provides an excellent overview of the field, it would be suitable reading in preparation for a course in human genetics, although it is not comprehensive enough to serve as a textbook for such a course. It may be of particular interest to the physician who frequently has responsibility counseling parents, because it will give him a quick and complete overview of the subject in language which he can in turn use directly in dealing with the parents. It will also give him the additional advantage of being significantly ahead of the genetics courses that the parents may be studying in random issues of current popular magazines. If this book can be considered a harbinger of other books in this series, "Perspectives in Medicine," physicians should keep their eyes on that series for providing a gentle introduction to the intrigue of medicine to members of their families and to other young people in the community who might venture into one of the medical or paramedical fields. The physician can safely recommend "Heredity, Disease & Man" to any high school or college student who expresses an interest in the medical areas; for the book will intrigue, delight, and inform him without frightening him with technicalities, abstruse and difficult language and formulas.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

INTRODUCTION TO PROTOZOOLOGY by Menwell; Dover Publications, Inc., New York; Price: $4.00.

This is a very complete, comprehensive monograph on the study of protozoa. It comprises 28 chapters, the first 12 of which are related to the basic studies: ecology, morphology, nutrition, metabolism, etc. The remaining chapters deal principally with the classification and identification of the numerous species. The chapter on ecology is pertinent at the moment because of the current interest in the numerous types of contamination: "Natural purification depends primarily on the activities of a variety of microorganisms plus such agencies as oxidation reduction and sunlight. The protozoa make a dual contribution. Some, such as bacteria feeders, tend to reduce the bacterial contact; others promote oxidation by the liberation of oxygen as a byproduct of chlorophyll synthesis. The most active consumers of bacteria are probably the vorticellids.

Carl O. Rice, M.D.
Minneapolis, Minnesota

COMMUNITY RESPONSE TO ALCOHOLISM AND HIGHWAY CRASHES, 1970, Highway Safety Research Institute, The University of Michigan, $6.50.

and

THE ALCOHOL-IMPAIRED DRIVER AND HIGHWAY CRASHES, OCTOBER 1970, Minnesota Department of Public Safety, St. Paul, Minnesota.

There is a rising tide of awareness of the terrible contribution that alcoholism makes to highway injuries. A very thorough review of possible community action was carried out in a national symposium at Ann Arbor in 1969. The proceedings of this conference make hard reading but provide a very complete report of the stage of thinking in our country at this time. It is an excellent compilation for anyone who wishes to engage himself in a serious effort to improve this problem in public health.

The second pamphlet is a sleeper, a little gem of current knowledge produced by the Minnesota Department of Public Safety. In eighty-three pages of lucid and tight writing, the whole subject is dissected and illuminated. All of the hearsay and the near-truths and the half-truths of the usual discussions of this problem are reduced to simple facts by this precise little booklet. What do they do in Sweden? Precisely what is implied consent? What does the dramshop law provide? What distinguishes a social drinker, a problem drinker, a problem driver, an alcoholic? Does chemical testing for alcohol violate the First Amendment? How much intake is required to produce impairment?

This booklet is a must for any physician treating trauma, for any physician rendering primary care to people over the age of twelve.

The Minnesota State Medical Association participated in this booklet through the person of Dr. James Halvorson. He and the other contributive experts are dedicated to reduction of the drinking-driver accident toll. Their booklet is available free, by request to the Minnesota Department of Public Safety, St. Paul 55101. I highly recommend it to every thoughtful physician who treats either trauma or people.

S. R. Maxeiner Jr., M.D.
Minneapolis, Minnesota

A PHYSICIAN'S LIVING THOUGHTS by Carl Thenebe, M.D.; Philosophical Library, N.Y.; 161 pages; $4.95.

This small book, dealing with the thoughts of a physician, is divided into 16 pauses (chapters). He deals with numerous phases of life—its philosophies, morals, ethics, principles, emotions, and its health. It can provide numerous moments of relaxation while at the same time providing intellectual stimulus.

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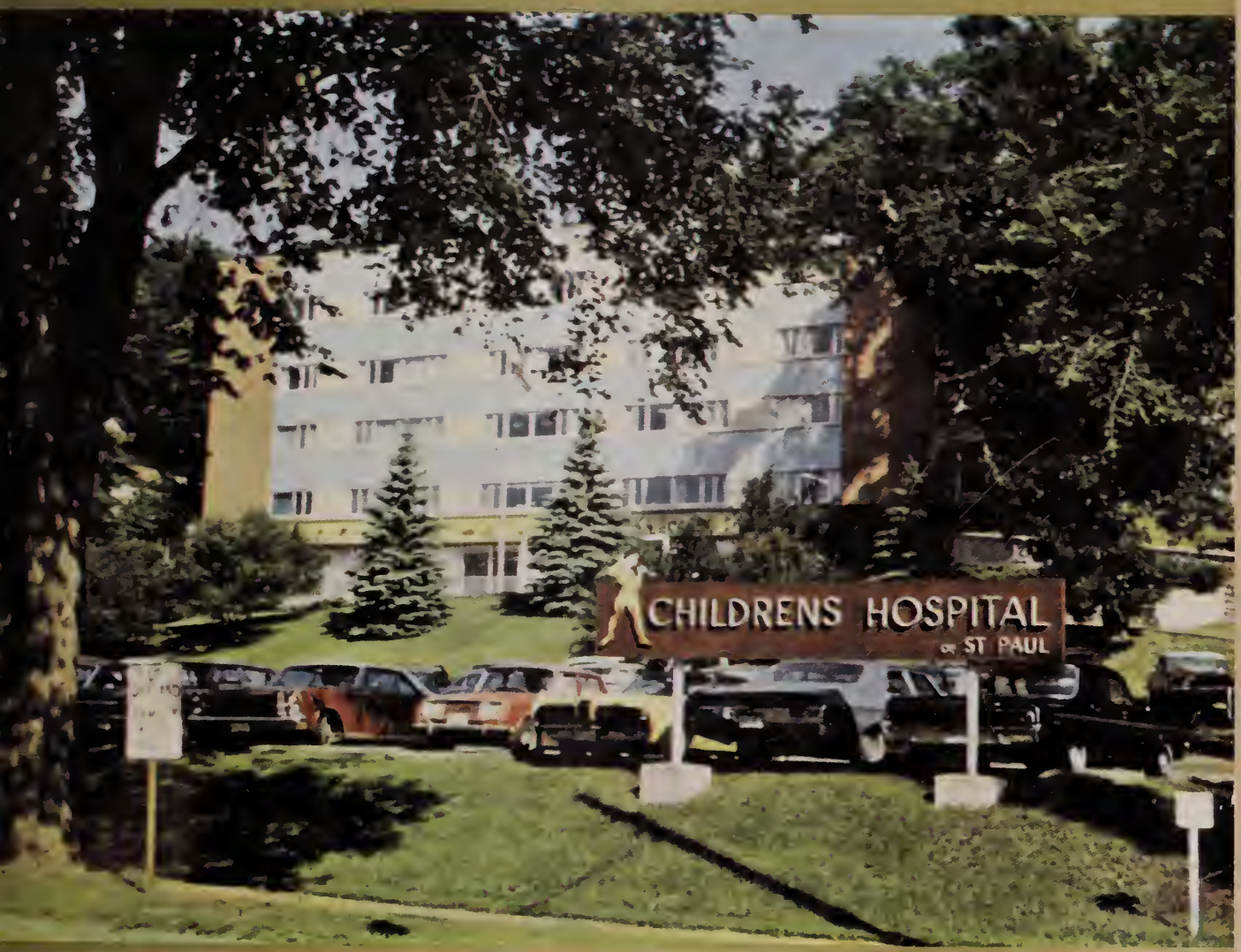
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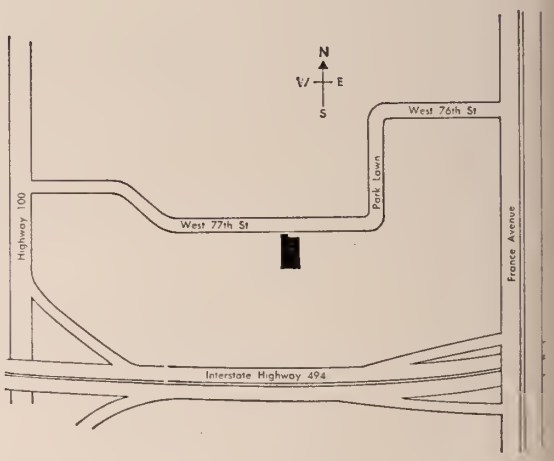
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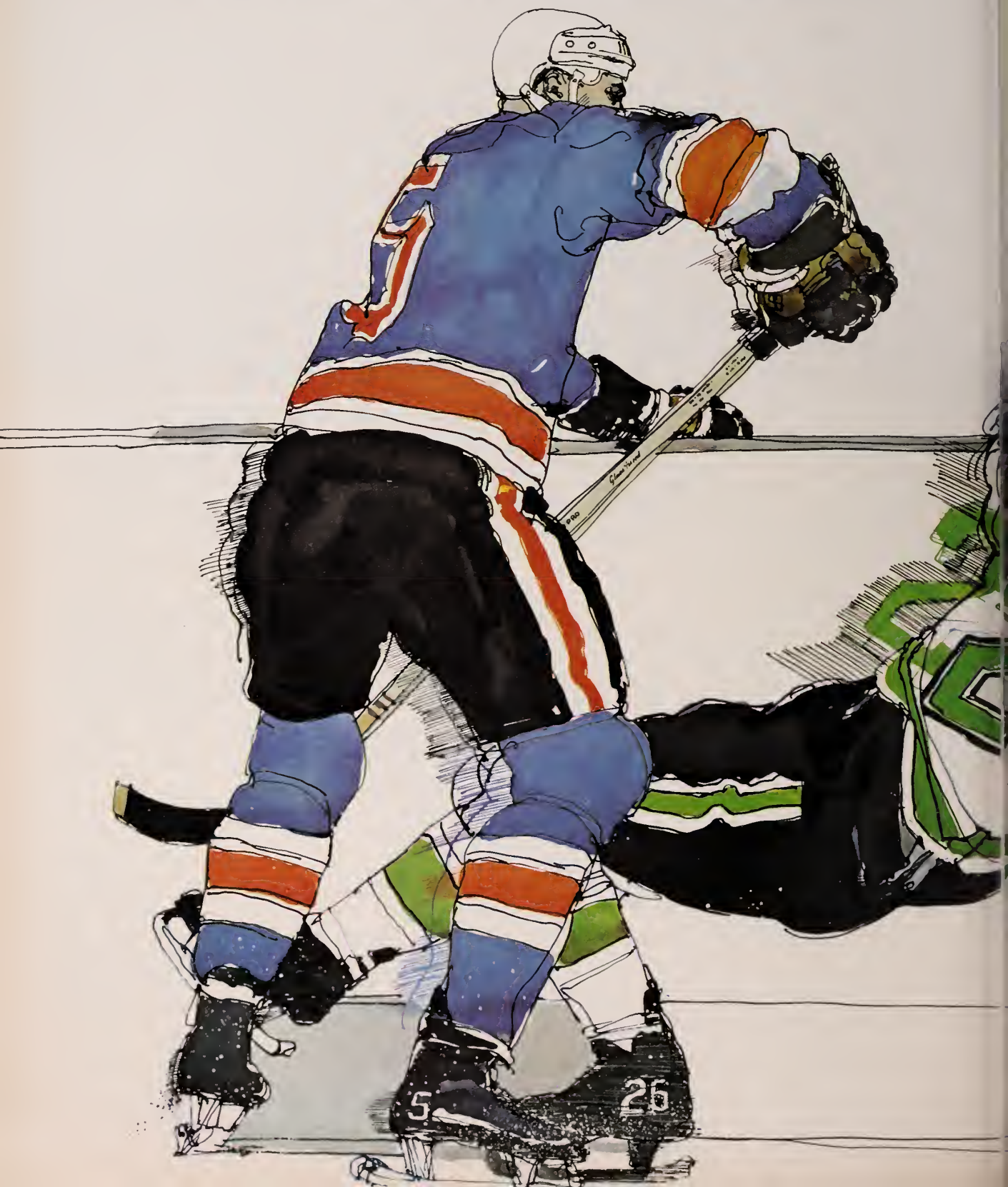
mportant Note: This drug is not a simple analgesic. o not administer casually. Carefully evaluate patients efore starting treatment and keep them under close upervision. Obtain a detailed history, and complete hysical and laboratory examination (complete emogram, urinalysis, etc.) before prescribing and at equent intervals thereafter. Carefully select patients, voiding those responsive to routine measures, con- raindicated patients or those who cannot be observed equently. Warn patients not to exceed recommended osage. Short-term relief of severe symptoms with ne smallest possible dosage is the goal of therapy. osage should be taken with meals or a full glass of ilk. Patients should discontinue the drug and report mmediately any sign of: fever, sore throat, oral sions (symptoms of blood dyscrasia); dyspepsia, pigastric pain, symptoms of anemia, black or tarry tools or other evidence of intestinal ulceration or emorrhage, skin reactions, significant weight gain or dema. A one-week trial period is adequate. Discon- nue in the absence of a favorable response. Restrict eatment periods to one week in patients over sixty. *ndications:* Acute gouty arthritis, rheumatoid arthritis, heumatoid spondylitis.
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Warnings: Age, weight, dosage, duration of therapy, xistence of concomitant diseases, and concurrent otent chemotherapy affect incidence of toxic reac- ons. Carefully instruct and observe the individual atient, especially the aging (forty years and over) ho have increased susceptibility to the toxicity of the rug. Use lowest effective dosage. Weigh initially npredictable benefits against potential risk of severe, ven fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.
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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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President's Letter

Partnership In Medical Education

In September, 1972 approximately 225 medical students will begin medical training in Minnesota. This has been achieved by opening two new medical schools: one at Rochester and one at Duluth, as well as the increased enrollment of our present medical school at the main campus.

This increase in potential doctors for Minnesota did not just happen. A great deal of effort was needed from our medical educators, the practicing physicians and our legislators to accomplish this expansion.

Now that this expansion has taken place, the faculties of the three medical schools face a monumental challenge to provide a quality and meaningful training program for these students. This must be done in their undergraduate as well as their postgraduate training programs. The private practicing physician in Minnesota must also assume an active role in helping to provide opportunities for these medical students and residents. He must be willing to participate in new programs as well as educational programs already established.

The Rural Physicians' Associate Program is an example of a new program already in operation. This program has allowed 23 medical students to spend one year of their education working with a rural physician. This program is now six months old and from all appearances, it is an overwhelming success. The student is finding rural Minnesota communities attractive and the learning opportunities to be exceptional. The physicians are enthusiastic and willing to make the sacrifice necessary to insure success of the program and finds the medical student to be intellectually stimulating. The faculty of the Family Practice Department has assumed the responsibility for providing one of their staff members as well as a faculty member from one of the other specialty departments of the University of Minnesota Medical Schools to visit once a month each area where a student is in training. The student presents interesting cases to the visiting faculty and all of the area doctors attend these sessions making them a true educational experience.

This new program is a perfect example of how medical education can be an ongoing achievement not only for the student but for the faculty members and the rural physicians. The more opportunities, such as the Rural Physicians' Associate Program, that exist, the better the medical care will be for residents of Minnesota.

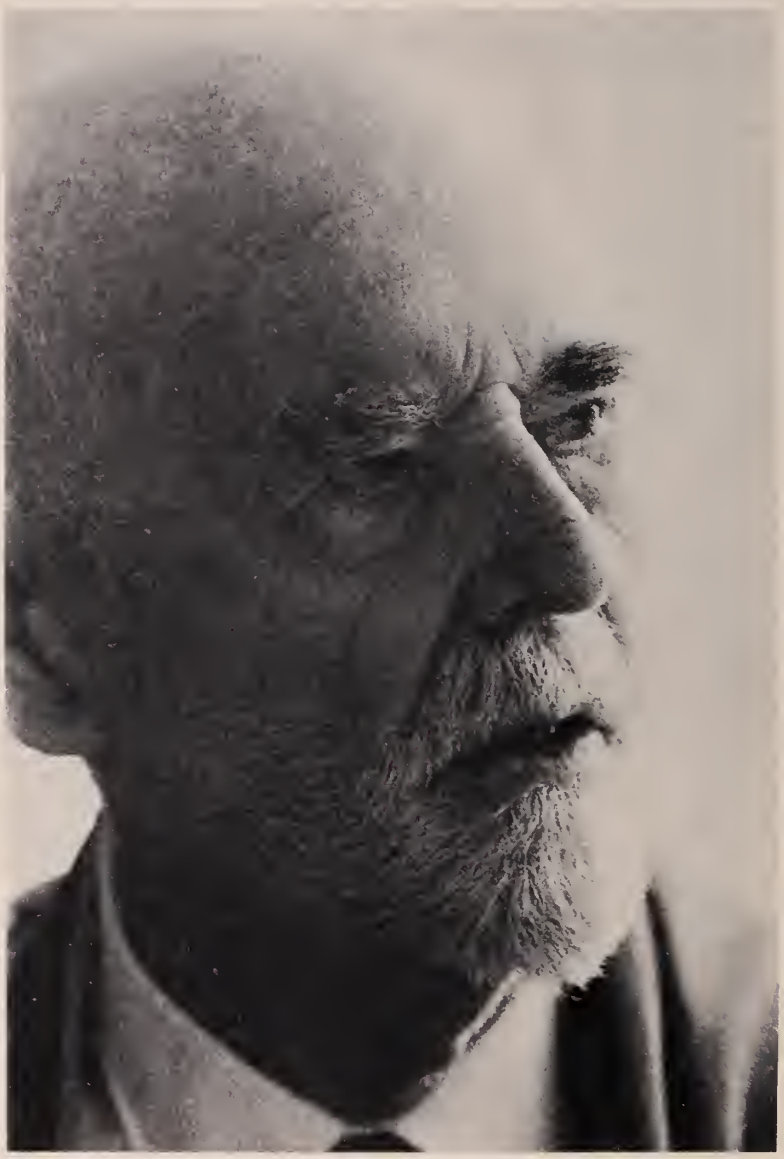
With the increasing number of students both on an undergraduate and postgraduate level, we must continue to provide new and stimulating programs for these young men and women. These programs must be a product of close cooperation of all the physicians of the state. We have just begun this partnership in medical education which I feel is so urgently needed. The potential benefits of this partnership are unlimited.

By developing new programs the quality and availability of medical care to our patients in Minnesota will indeed continue to improve.

Robert T. Kelly

President
Minnesota State Medical Association

Dedicatory



Walter Reeve Ramsey, M.D.

Dr. Ramsey, who graduated from medical school in 1896, and who in 1902 became the first physician in this area to limit his practice to pediatrics, incorporated The Childrens Hospital in 1923. Almost half a century later, on November 8, 1971, Dr. Ramsey celebrated his 99th birthday.

The Childrens Hospital Special Issue

Hugh J. Williams, M.D., Guest Editor
Charles W. Jarvis, M.D., Guest Editor

A Childrens Hospital*

—is a place where infants and children may go and receive the best medical and surgical care known to science.

—must have a staff of physicians, surgeons, nurses, and a personnel especially trained in the field of children.

—need not be large, but must be a model in the things pertaining to the health and welfare of children.

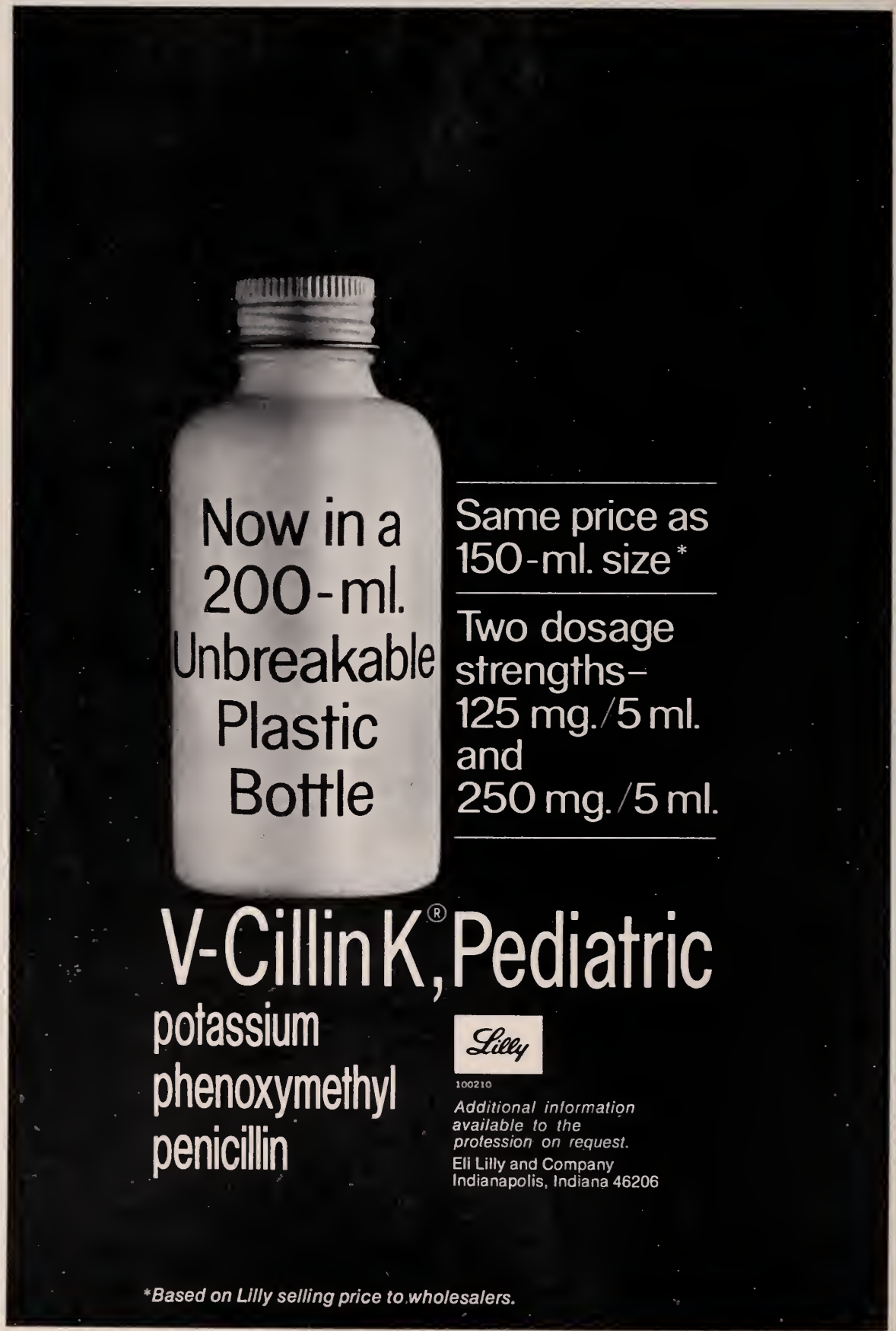
—must be a center of education for physicians, nurses, and the public in the health and well-being of children.

—should be regarded as "a vital institution of health and education in the community," which must be subsidized.

—must maintain its identity, dedicated not only to the best medical and surgical care of children, but to research and the dissemination of knowledge in the things pertaining to the health of children.

Walter Reeve Ramsey, M.D.

*History of the Childrens Hospital, St. Paul, Minnesota. Published privately by Dr. Ramsey, 1954 (21 pages). Second and revised edition published in 1963 (18 pages).


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Relapse of Meningitis after Ampicillin Therapy

KRISHNA M. SAXENA, M.D.* AND DAVID MAAS, M.D.*

AMPICILLIN HAS BEEN considered the drug of choice for the treatment of meningitis due to Hemophilus influenzae.[1,2] There is no doubt that it is effective and relatively nontoxic and has the advantage of being a bactericidal rather than a bacteriostatic drug. The commonly recommended dose is 150-200 mg/kg/24 hours[1-4] given in four to six divided doses intravenously, and most cases respond well to this dosage.[3,4]

The penetrance of ampicillin into the cerebrospinal fluid is rather poor and the concentrations, even during the acute stage of meningitis, range from approximately 3% to 30% of the serum levels.[3,5] As the inflammation of the meninges subsides, the permeability decreases, and levels in the spinal fluid decrease further. Thrupp et al. found a mean cerebrospinal fluid-serum ratio of 36% on the third day of treatment and 12% on the tenth day or later, with a range of 0 to 100%.[6] Hence, some authors have recommended a higher dosage, from 200-400 mg/kg/24 hours.[7] Over the last four years, we have treated all cases of H. influenzae meningitis with ampicillin in a dose of 400 mg/kg/day. Even with this larger dose we have seen relapse in a child after therapy had apparently produced a clinical and bacteriological cure. In several other children we have observed a delayed clinical response or persistence of fever on ampicillin, which responded promptly within 24 to 48 hours when the antibiotic was changed to chloramphenicol. However, it should be emphasized that the vast majority of approximately 150 children with meningitis treated at The Childrens Hospital during the last four years responded well to ampicillin therapy.

Case Report

First Admission

A four-month-old white male weighing 9 kg., was admitted to Childrens Hospital on November 3, 1969. His illness began two weeks prior to admission with cough, which became progressively worse for seven to eight days. He then developed a fever of 102.8°F and was admitted to another hospital on October 28, with a diagnosis of tracheobronchitis. He was given ampicillin, 125 mg. q.6 hourly I.M. (55 mg/kg/day).

The following day the patient had a generalized seizure. His temperature returned to normal by October 31. At that time he was asymptomatic, and oral ampicillin was started in the same dosage. The next day he again developed fever and, on November 2, the antibiotic was changed from ampicillin to triacetyloleandomycin. He remained febrile and was transferred to Childrens Hospital on November 3.

Physical Findings

On admission the child was found to be lethargic, semiconscious, and responsive only to painful stimuli. He had nuchal rigidity, a firm, bulging fontanelle and a temperature of 102.8°F. The chest, heart and abdomen were normal. No evidence of otitis or pharyngitis was found and the child appeared to be well hydrated. Transillumination of the head was within normal limits.

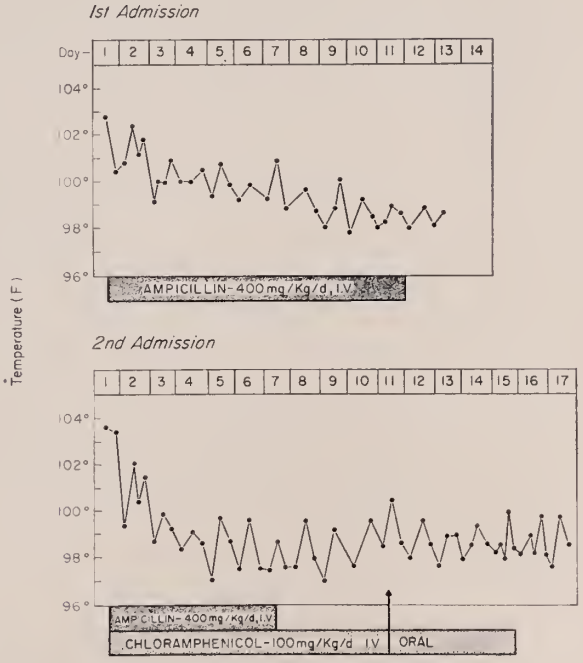


Fig. 1—Hospital course of Patient #1.

*From the Department of Pediatrics, University of Minnesota and The Childrens Hospital, Inc., St. Paul, Minnesota.

His WBC count was 22,000 with 83% neutrophils, 11% lymphocytes and 6% monocytes. Lumbar puncture revealed a cloudy cerebrospinal fluid which was positive for gram-negative pleomorphic rods on smear.

Cerebrospinal fluid from the initial lumbar puncture grew H. influenzae organisms which were resistant to ampicillin by disc sensitivity. Tube dilution studies could not be done. A blood culture drawn at the same time grew H. influenzae group B which was sensitive to ampicillin by the disc sensitivity test.

Treatment

Therapy was started with a loading dose of 1.0 gm. ampicillin intravenously, followed by 400 mg/kg/day in six divided doses. The patient responded well clinically; he was alert and had decreased neck stiffness the following morning. His temperature fell by lysis over several days and was normal by the eighth day of admission (Figure 1). Nuchal rigidity disappeared by the fifth hospital day and his appetite returned to normal. Repeat lumbar punctures done on the fourth and eighth hospital days showed normal sugar and protein and were negative for organisms by smear and culture (Table). He continued to do well clinically and ampicillin was discontinued at the end of the eleventh hospital day, seven days after the cerebrospinal fluid had returned to normal and three days after the temperature became normal. He was discharged well on the thirteenth day.

Second Admission

The child apparently did well at home for the next four days. On the fifth day after discharge, he developed a temperature of 102°F and became very irritable. He was readmitted the following day with a temperature of 103.6°F. Physical examination showed irritability, listlessness, and mild neck stiffness. His fontanelle was soft and flat. Head circumference was the same as before (42 cm.) and transillumination was negative. The rest of the physical examination was normal. His WBC count was 23,000/cmm. with 82% neutrophils, 16% lymphocytes, and 2% monocytes. Lumbar puncture yielded only a small amount of cerebrospinal fluid; therefore cell count and chemistries could not be done. However, a smear showed pleomorphic gram-negative rods and the culture was positive for H. influenzae group B. He was again given a loading dose of 1.0 gm. ampicillin intravenously, followed by 400 mg/kg/day in six divided doses plus chloramphenicol, 100 mg/kg/day in four divided doses.

The day following admission the child was still listless, but by the third day he was afebrile, alert and eating well. On the fifth day his WBC count was 9,300/cmm. with 12% neutrophils, 79% lymphocytes, 6% monocytes and 3% eosinophils. The child was clinically normal for the rest of his hospitalization. Repeat lumbar punctures done on the third, eighth and seventeenth hospital days were negative on smear and culture. The other findings are shown in the Table.

Ampicillin was discontinued after six days but chloramphenicol was continued intravenously for 10 days and then orally in the same dose for another five days. He was discharged after 17 days of hospitalization. Followup examinations at one week, six weeks and six months after discharge were completely normal.

Discussion

The studies of Mathies[4] and of Barrett et al.[3] have established ampicillin as the drug of choice for H. influenzae meningitis. No strains resistant to ampicillin have been reported to date.[8] In-vitro studies show almost all strains sensitive to levels greater than 0.78 mg/ml. and most to levels greater than 0.39 mg/ml. of ampicillin.[3,9] The levels of ampicillin in the cerebrospinal fluid, after 150 mg/kg/24 hours were given intravenously every four hours, ranged from 0.03 to 7.00 mg/ml.,[6] but in the majority of cases they reached bactericidal levels. Although a disc sensitivity test does occasionally show resistance to

TABLE
Cerebrospinal Fluid Findings

Date	WBC/c.mm.	PMN%	Mono%	Protein mg%	Glucose mg%	Smear	Culture	Remarks
First Admission								
11-3	625	75	25	44	29	Pleomorphic gram neg. rods	H. Influ.	Blood culture - H. Influenzae Group B sensitive to ampicillin
11-6	106	20	80	58	40	Neg.	Neg.	
11-10	31	40	60	38	38	Neg.	Neg.	
Second Admission								
11-19						Pleomorphic gram neg rods	H. Influ. Group B	H. Influenzae in C.S.F. sensitive to ampicillin by disc.
11-21	1,019	41	59	36	30	Neg.	Neg.	
11-26	41	0	100	32	44	Neg.	Neg.	
12-5	23	4	96	21	41	Neg.	Neg.	

ampicillin, the more reliable tube dilution test has not borne this out.[8] Nevertheless, at least 10 cases have been reported in the literature where the child either did not respond well to treatment or had a relapse of meningitis during or after the completion of a course of therapy with ampicillin.[10-18]

Seven of the 10 children has been treated with ampicillin in a dose of 200 mg/kg/day or less. The other three received between 200-300 mg/kg/day.[16,17] In our case the dose was 400 mg/kg/day for the entire period of therapy.

Sequestered Areas of Infection

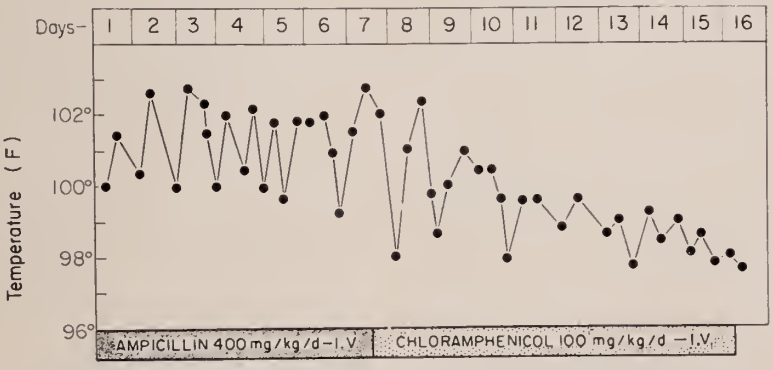
It is conceivable that localization of infection in a sequestered area may hinder penetration of the antibiotic and allow organisms to proliferate. Subdural effusions or 'orbital cellulitis' was found in several reported cases.[10,15,17] No such localization or latent focus of infection, e.g., otitis, mastoiditis, subdural effusion, was observed in our patient. Nor did the child manifest any other complication of H. influenzae infection to acount for the relapse of meningitis.

Approximately 150 children with H. influenzae meningitis have been treated with ampicillin during the last four years at The Childrens Hospital.[19] Because of the relatively poor penetrance of ampicillin into the cerebrospinal fluid, we have routinely used a dose of 400 mg/kg/day intravenously in four to six divided doses. In five children, chloramphenicol was used when the response to ampicillin was unsatisfactory.

In the first child described in this report, chloramphenicol was given for the treatment of relapse of meningitis. In two other children, the temperature continued high for five to seven days despite the fact that the cerebrospinal fluid cell count, sugar and protein showed improvement. No other complication or cause for fever was found and the temperature dropped to normal within two days of starting chloramphenicol. In two additional patients, although the cerebrospinal fluid cell count and protein decreased, the sugar persisted at a very low level (5 and 8 mg/100 ml. respectively) and temperature remained high for five to six days after ampicillin therapy was begun. The blood sugar was normal in both cases. Therapy was changed to chloramphenicol and, within 24 to 48 hours, the cerebrospinal fluid sugar rose up to normal in both patients. It must be pointed out that in all these four patients, the smear and cultures of cerebrospinal fluid, as well as blood cultures, became and remained negative after the initial ampicillin treatment.

Chloramphenicol

In light of the preceding observations, we feel that ampicillin is effective in most cases of H. influenzae meningitis in children and must be the initial drug used. However, treatment failures do occasionally occur; chloramphenicol may then have an important place in the treatment of such cases.



C.S.F.			
CELLS	6050/cmm	296	19
PMN / MONO	93 / 7 %	30 / 70 %	12 / 88 %
PROTEIN	98 mg%	96	30
SUGAR	15 mg%	55	92
SMEAR	H Influ.	Neg.	Neg.
CULT.	H Influ.	Neg.	Neg.

Fig. 2—Hospital course of Patient #2 (See discusssion).

Dose

For obtaining optimal response to ampicillin, a relatively high dose of 400 mg/kg/day intravenously (given in four to six divided doses) seems to be indicated. We have not encountered any significant side effects from this dose. Therapy should be prolonged, especially if the child had been ill for several days before diagnosis was made or had received partial or inadequate antibiotic treatment for other illnesses.

Dangers

The dangers associated with chloramphenicol are well known. Nonetheless, in certain special circumstances its use may be justified. One of its main advantages is its ready diffusibility into the cerebrospinal fluid. The following conditions should be considered as possible indications for chloramphenicol in patients with H. influenzae meningitis:

1. Hypersensitivity to penicillin. 2. Failure of cerebrospinal fluid sugar to come up to normal after three days of adequate therapy with ampicillin in the presence of normal blood sugar. 3. Failure of temperature to return to normal within five to six days in the absence of complications. 4. Relapse of meningitis after successful response to therapy with ampicillin.

Conclusion

A patient with H. influenzae meningitis who developed a relapse after ampicillin therapy was treated with chloramphenicol during the relapse and responded promptly. At six months follow-up, he was quite normal. While ampicillin is the drug of choice in H. influenzae meningitis, chloramphenicol may be indicated in certain special circumstances.

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Maintenance Fluid Requirements

of Small Infants

JOHN W. REYNOLDS, M.D.*

THE MAINTENANCE water requirement for the patient under treatment is defined as that required to replace the insensible water loss (skin and respiratory tract evaporation) and urine formation in the afebrile patient at bed rest, receiving nothing by mouth, and with minimal alimentary tract losses. It is also assumed that the patient is receiving enough calories, usually via intravenous glucose, to prevent ketosis and to limit the catabolism of endogenous protein.

Fluid Requirements and Metabolic Rates

Throughout most of childhood and adulthood, the water and electrolyte requirements are proportional to the body surface area, 1500-2000 ml. per square meter per day. However, the use of body surface area does not have a good physiologic basis[1] and its usefulness depends on the generally good correlation of the metabolic rate with the surface area. Unfortunately, this correlation with surface area does not hold for newborn infants, as will be discussed below.

Insensible Losses

The metabolic rate, an expression of the magnitude of heat production, is the primary determinant of maintenance water requirements. Insensible water loss through evaporation from the skin and respiratory tract is a major means of ridding the body of heat and thus maintaining a constant body temperature. At all ages, approximately 24% of basal heat loss is through evaporation. The metabolic rate and the volume of the insensible losses are closely related in that the insensible losses are approximately 45 ml. per 100 Calories expended. This volume includes 30 ml. as skin losses and 15 ml. as respiratory tract losses.

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See editorial, page 137.

Urine Volume

The kidneys are required to excrete about the same load of solutes, mainly protein breakdown products such as urea, per unit of heat production at all ages. Therefore, the metabolic rate determines to a great extent the amount of endogenously produced solute load presented to the kidneys under basal conditions. As water is required for the excretion of these solutes, and the greater the solute load, the larger will be the volume of water required at any given urine osmolality, the metabolic rate is an important determinant of urine volume.

The renal solute load during parenteral therapy in a basal state is approximately 20 mOsm per 100 Calories.[2,3] For this amount of solute to be excreted in a urine of the same osmolality as plasma, 285 mOsm per l., 70 ml. of water would be required. Thus, the water requirement for formation of nonconcentrated urine is about 70 ml. per 100 Calories expended. If urinary concentrating ability is intact, less water would be needed, but in many ill infants the ability to produce a urine osmalality above that of plasma may be impaired. Small amounts of water may be lost in normal stools but are probably balanced by the water of oxidation, 12 ml. per 100 Calories expended, which is produced in the body as a by-product of the metabolism of foodstuffs or products of body catabolism.

Summary

The maintenance water requirements in a basal state are 45 + 70 = 115 ml. per 100 Calories expended. Because most patients, including sick infants, are not resting quietly at all times and thus are not in a truly basal state, the requirement should be increased by 50%. Under the conditions described above, the requirement

would thus be increased to 170 ml. per 100 Calories. This increase will cover variations in activity level, small amounts of sweating which may occur, and variations in the production of the endogenous renal solute load.

Neonatal Metabolic Rate

In the first week or weeks, the caloric expenditure per square meter of body surface area and per unit of body weight is much lower than later in life. This has been known for many years,[4] but the physiological bases, a difference in body composition and a lower metabolic rate of the major body organs, were not understood until recently.

Body Composition

In newborn infants, especially in prematures, metabolically inactive water makes up a much higher proportion of the total body mass than in the older infant or child.[5] The proportions of water and the various metabolically active tissues change rapidly during the neonatal period, leading to changing metabolic rates per square meter or per kg. depending on the age of the infant and his size and maturity at birth. The body fraction whose variation most influences the changing metabolic rate is the extracellular fluid.[6]

Lower Metabolic Rate of Major Organs

The other reason for the relatively low metabolic rate of the newborn infant is a lower metabolic rate per kg. of brain, liver, heart and kidney before one month of age than after.[7] Since these organs are the main sites of oxygen consumption in the newborn, their metabolic rates essentially determine the metabolic rate of the whole infant.

Summary

The low metabolic rate per M^2 or per kg. in the neonate is due to the high fraction of the body mass made up by water, and therefore the relatively small fraction of body mass made up by actively metabolizing organs; and the relatively low metabolic activity of these organs as compared with their metabolic rates one month later. The increasing metabolic rate per M^2 or per kg. during the first one to two months of life, therefore, is due to the increasing proportion of the weight made up by metabolically active organs and the increasing metabolic activity of the organs themselves.

Oxygen Consumption and Calorie Production

Calories produced can be calculated from O_2 consumption, using the average value of 4.83 Calories per liter of O_2 consumed. At an abdominal skin temperature of 96-96.5°F (the neutral range), the newborn in the first few days of life can be considered to be in a basal state and the O_2 consumption is 4.5-5.5 ml./kg./min. in premature, full-term infants and infants with intrauterine growth retardation.[8,9] The O_2 consumption rises with increasing age in all infants, is consistently lowest in the smallest prematures and is highest in infants with intrauterine growth retardation. At age seven to 14 days, the O_2 consumption is roughly 7 ml./kg./min. and by one to two months is about 9 ml./kg./ in prematures.[9] These figures are in contrast to findings in full term infants of O_2 consumption of about 7 ml./kg./min. from two weeks up to one year of age.[10] O_2 consumption data have been transferred into values for heat production (Cal./M^2/hr.) by Hey and Katz[11] who showed that in prematures of 1.8-2.1 kg. birthweight, heat production rose from about 22 Cal./M^2/hr. on Day one to 25 Cal./M^2/hr. on Day 10 and 30 Cal./M^2/hr. on Day 20. In smaller prematures, of 0.9-1.2 kg. birthweight, the heat production values at the same ages were 16, 20, and 25 Cal./M^2/hr.

TABLE

			Basal Metabolic Rate			Maintenance volume based on 170 ml per 100 Cal. expended	
Wt. (kg.)	S.A. (M^2)*	Age	Metabolic Rate	Cal./kg./d.†	Cal./M^2/d.†	ml/kg./d.	ml/M^2/d.
1.0	0.10	2d.	5 ml. O_2/kg./min.	35	350	60	600
1.0	0.10	2d.	18 Cal/M^2/hr.	43	430	73	730
2.0	0.16	2d.	22 Cal/M^2/hr.	42	530	71	900
3.0	0.21	2d.	5 ml. O_2/kg./min.	35	500	60	850
3.0	0.21	10d.	7 ml. O_2/kg./min.	49	700	83	1190
2.0	0.16	21d.	9 ml. O_2/kg./min.	62	780	105	1325
2.5	0.18	21d.	30 Cal/M^2/hr.	52	720	88	1220
5.0	0.30	2mo.	7 ml. O_2/kg./min.	49	820	83	1400
8.0	0.40	6mo.	7 ml. O_2/kg./min.	49	980	83	1670
70.0	1.7	40yr.	5 ml. O_2/kg./min.	35	1440	60	2450

*Surface area (M^2) = 0.1 x wt. $(kg.)^{2/3}$

†Liter of O_2 consumed yields 4.83 calories.

Causes of Increased Oxygen Consumption

Most importantly, a fall or rise in the temperature away from the neutral range leads to increased O_2 consumption. A fall in the skin temperature leads to an increased heat production and O_2 consumption, but this is not reflected in an increased evaporative water loss unless the baby begins to cry.[12] The lack of an increase in evaporative water loss is probably due to peripheral vasoconstriction, acting as a heat conserving mechanism. Thus, the increased rate of metabolism with cold stress is not associated with a parallel increase in water requirement. Infants showing intrauterine growth retardation have a higher O_2 consumption per kg. than other infants matched for both weight and gestational age.[9,13] This may be due to a decreased body water content and thus a preponderance of metabolically active organs, and perhaps due to a heightened metabolic activity as a post-malnutrition recovery phenomenon. There is much variability among such growth retarded infants but the increase in O_2 consumption in one series was 17% over that predicted from the weight, with many infants showing a 30-50% increase over predicted values.[13]

Causes of Decreased Oxygen Consumption

Oxygen consumption may be significantly low in severe hypoglycemia (4.0-4.3 ml./kg./min.) and in severe icterus with lethargy.[14] In infants with the respiratory distress syndrome, O_2 consumption is low (mean - 4.3 ml./kg./min.) during the first two days, then rises to above normal levels of 8-10 ml./kg./min. at four to five days, before return to normal (5-7 ml./kg./min.) at seven days.[15] Thus, during the early period of marked cardiorespiratory effort, the O_2 consumption is low.

Recommendations

The following examples (Table) of the calculation of maintenance water needs are based on the preceding discussion and the data presented. Hopefully, the physiological bases of the calculations are clear enough that the reader may modify the figures if new metabolic rate data become available.

Several recommendations can be derived from the examples presented:

1. In the first two to three days, the maintenance water requirements are 60-70 ml./kg./d.
2. Water needs rise through the first week and level off at 80-90 ml./kg./d.
3. In infants with intrauterine growth retardation and some prematures one to two month old, water requirements may go to 100-110 ml./kg./d.
4. The use of the common rule of 1500-2000 ml./M^2/d. may lead to significant overhydration in infants under one month of age.

The water solutions administered intravenously in the neonatal period should contain 10% glucose because of the frequent occurrence of hypoglycemia in ill newborns. An electrolyte free solution is administered for the first two to three days of life because ill newborns commonly require $NaHCO_3$ treatment of metabolic acidosis and Na^+ overloading is a frequent problem. Thus, they do not need further Na^+ as part of the maintenance fluids. Serum K^+ is frequently high as a result of neonatal hypoxia and acidosis and thus K^+ administration is not advised. After three days of age, the fluids used should contain approximately 20 meq. per 1. Na^+ and 20 meq. per 1. K^+ as the chlorides[2] or a portion of the anions may be a metabolizable organic anion such as acetate, lactate or bicarbonate.

Conclusion

Maintenance water and electrolyte requirements for infants in the first month of life cannot be calculated from the ml. per M^2 or ml. per kg. values used in planning therapy for older infants and children. Differences in body composition and metabolic activity of major body organs between newborns and older infants make essential the use of caloric expenditure, or metabolic rate, as the basis for calculating fluid requirements. Recent extensive data on caloric expenditure of premature, growth retarded, and full-term infants allow a more precise definition than previously possible of neonatal requirements. Using the value of 170 ml. required per 100 calories expended, neonatal maintenance water requirements are 60-70 ml./kg./d. in the first two to three days and rise to 80-90 ml./kg./d. by one week.

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See page 176 for balance of reference 4-15.

Urinary Bladder Capacity

The Clinical Importance in Children

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EDWARD J. RICHARDSON, M.D.

WE SEE TWO KINDS of voiding problems in children. Some void infrequently and are troubled with urinary tract infections; others without infections void too frequently and are troubled with numerous other urologic problems.[1] Presumably some of these symptoms are related to bladder size.

In 1968 we were particularly interested in the differential diagnoses of children having frequency, urgency sometimes to incontinence, and/or enuresis.[1] We found a variety of problems associated with these "small bladder" symptoms, but the number of patients actually having small bladders was difficult to assess since no normal values for bladder size at cystoscopy under general anesthesia were available for comparison. For this reason measurements of bladder capacity were made on 312 children referred for a variety of urologic complaints.*

Three useful observations are made from this data: (1) In the average the size of the bladder was found to be larger in children with urinary infections. (2) Over-sized bladders occurred as frequently in younger untrained children as in older children, suggesting that a larger bladder is congenital and not acquired through training or habit. (3) Children having so-called "small bladder" symptoms were seldom found to have small bladders. Patients with frequency, urgency, incontinence or enuresis or both were found to have a variety of urinary tract pathologies.

Materials and Methods

Bladder capacity was measured in 312 children during 338 consecutive cystoscopies under general anesthesia from December, 1968, to December, 1970 (Table 1). Twnety-six children did not have their capacity measured for one reason or other: when acute cystitis was found; when reflux with recent infection was known; when anesthesia was of inadequate depth; or when there was oversight on the part of the examiner.

TABLE 1
Reasons for Cystoscopy in 338 Children

	No.	Male	Female	Bladder Capacity Measured
Urinary Tract Infection	163	22	141	145
Sterile Urine with Bladder Symptoms	146	83	63	141
Sterile Urine with Other Problems (e.g., hematuria, abdominal pain, etc.)	29	22	7	26
	338	127	211	312

A pressure of 70 cms. of water was arbitrarily chosen to measure the bladder capacity. This pressure was in excess of normal resting and voiding pressure and, theoretically, measured the distensibility of the sol-gel material composing the bladder wall. The bladder can be distended more at higher pressures, but using pressures close to bladder rupture is clinically inadvisable. A pres-

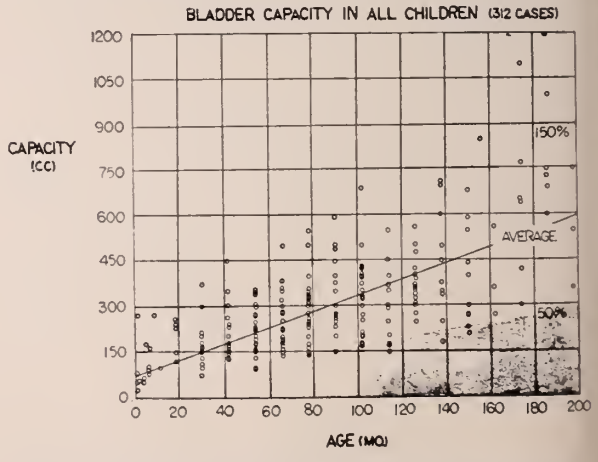


Fig. 1—Average capacity at age five years, six months is 250cc. There is an increment of approximately 30 cc. to bladder capacity per year of age.

*The values obtained are only meant to be useful for comparison until some investigator measures the bladder capacity in a sample of normal children.

See editorial, page 136.

sure of 70 cms. of water proved safe in all cases and served adequately for therapeutic dilation of the bladder in cases of interstitial cystitis.[1]

Results

Average Bladder Capacity

The average bladder capacity for all children under age one to sixteen is estimated by a line in Figure 1. The actual average capacity at each age is noted in Table 2 and compared with that estimated from Figure 1.

Large Bladders

We arbitrarily chose 150% of average capacity (the upper shaded area in Figure 1) to represent an unusually large bladder, but we suspect that a correlation with infrequent voiding history would reduce this percentage and increase the actual number of children having unusually large bladders. We are specifically avoiding a mathematical definition of "megacystis" in this paper. Ten percent of all children (32/312) had these large bladders, and *nearly all with large bladders had infections (28/32).* The decrease in resistance to infection with infrequent voiding is well known.[2]

In children with infections the percentage with oversized bladders age two and under was 28.6% (10/35) and 16.4% (18/110) in children who were trained. This suggests that we are born with and do not acquire unusually large bladders.

Small Bladders

Children having bladders 50% of average size (the lower shaded area of Figure 1) were arbitrarily said to have unusually small bladders. Only 14 of all 312 (about 5%) had truly small bladders, and in only four was this the only apparent cause of diurnal symptoms. Six children had enuresis only, three had interstitial cystitis with clearing of all symptoms after therapy and without change in bladder size, and one had a neurogenic bladder.

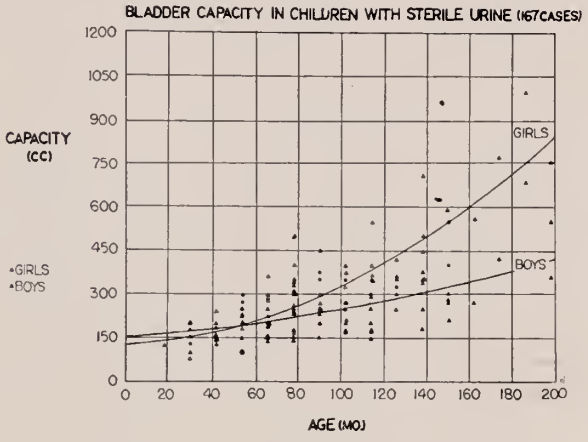


Fig. 2—There is little difference in bladder size until puberty is approached, at which time the rate of change in girls' bladders is greater than in boys. Quadratic equations have been used to emphasize this point.

TABLE 2
Bladder Capacity

	Under General Anesthesia At 70 cm. H_2O Pressure			Voluntary Retention (Starfield (3))	
Age	No.	(c.c.) Actual Average	(c.c.) Average Estimated from Figure 1	No.	(c.c.) Average
1	14	105	93		
1	6	205	124		
2	24	181	156		
3	30	196	187		
4	37	212	218		
5	31	239	249	22	249
6	35	286	279	15	240
7	24	315	311	21	291
8	28	299	342	20	291
9	18	325	373	30	345
10	19	378	404	32	390
11	14	401	435	18	363
12	13	415	467	22	435
13	3	397	498	23	525
14	7	648	529		
15	6	878	559		
16	3	553	591		
	312			203	

Sex and Bladder Size

A general average capacity is useful before puberty since girls and boys do not differ much before then. We have attempted to emphasize this visually in Figure 2 by using quadratic rather than linear equations for a line to best represent the data on each sex. Children with sterile urine were chosen for this comparison since, as noted above, an infected population introduces a predominately female group with unusually large bladders. This would act to distort the true relationship when one considers that the proportion of infected girls with large bladders (25/127 or 19.1%) was the same as the proportion of infected boys with large bladders (3/18 or 16.1%).

Average Bladder Capacity in Children Having Infection

As noted above, children having unusually large bladders are over-represented in the urologic population. They have a proclivity to develop infections because of infrequent voiding. Twenty percent (28/145) of children with infections had these unsually large bladders, thus raising the average size in this group (Figure 3). For instance, at age five the bladder averages about 75 cc. larger when infected than when sterile.

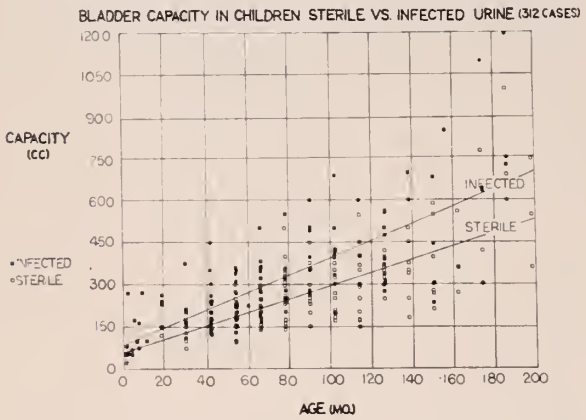


Fig. 3—The average capacity in children with infected urine is raised due to inclusion of a number of children having unusually large bladders. The children with excessively large bladders are over-represented in a urologic series by their proclivity to acquire a urinary infection due to infrequent voiding.

Average Bladder Capacity in Children Having Sterile Urine

This group consisted of 167 children. Only 26 had no bladder symptoms and were usually investigated for asymptomatic hematuria. The other 141 had diurnal symptoms of frequency, urgency sometimes to incontinence ("small bladder" symptoms) and/or enuresis (Table 3). The average capacity in this group was about 14% less than the general average. Ten percent (14/141) of children having sterile urine and bladder symptoms had unusually small bladders and, as noted above, in only four of them did this alone seem to explain their diurnal symptoms.

TABLE 3
Problems Found In Children Having Bladder Symptoms With Sterile Urine

	No.	Male	Female
1. Bladder Capacity Measured			
A. Diurnal Symptoms			
Intersitial cystitis	34	19	15
Ureteral reflux	22	15	7
Small meatus	4	3	1
Small bladder	4	2	2
Detergent urethritis	3	1	2
Neurogenic bladder	1	0	1
Obstruction (valves)	1	1	0
Polyp on veru	1	1	0
Left hydronephrosis	1	1	0
Diagnosis obscure	32	12	20
B. Nocturnal symptoms only			
Enuresis without pathology	36	23	13
Enuresis with ureteral reflux	2	1	1
	141	79	62
2. Bladder Capacity Not Measured			
A. Diurnal Symptoms			
Ureteral reflux	2	2	0
Small urethral meatus	1	1	0
Neurogenic bladder	1	0	1
Bladder diverticulum	1	1	0
B. Nocturnal Symptoms Only	0	0	0
	5	4	1

Discussion

The data suggest that it is not good to be born with too large a bladder, because if one voids infrequently the chances of infection are increased. Cox and Hinman,[4] O'Grady and Cattell[2] and Boen and Sylvester[5] have clearly shown the decrease in urinary tract resistance to infection associated with infrequent voiding. Lapsides[6] has documented this important factor clinically in both adults and children. This study confirms the fact that patients with infections frequently have too large a bladder. In addition, this study shows that unusually large bladders occur in children age two and under. Large bladders in these younger children, found well before training is started, could mean that such bladders are congenital and not acquired through laziness, poor training habits, or cultural expectations, as we have recently seen reported in the popular press.

A pattern of care for a child with urinary tract infection is not complete unless the bladder capacity and consequent voiding pattern are known. At least 20% have unusually large bladders and an unknown percent, an inadequate fluid intake. Where a bladder is large it is mandatory to check the child's urine for infection at frequent intervals until he or she can be trained to void with adequate frequency and to increase fluid intake. Training before age seven is not often possible. After age seven the susceptibility of these children to infections would indicate the need for continued surveillance of the urine at regular but longer intervals.

The 141 children with "small bladder" symptoms and sterile urine had a large variety of pathologies but not often an unusually small bladder (Table 3). For instance, a small bladder alone explained the symptoms in only four children; and a small bladder, though present in six children with enuresis, was unaccompanied with diurnal symptoms. Interstitial cystitis and ureteral reflux were the most frequent causes of an abnormal voiding pattern. The large group of 32 with diagnosis "etiology obscure" deserves attention: A few of them probably had interstitial cystitis but were unresponsive to a single therapeutic bladder dilation at 70 cms. of water, and by strict definition were grouped without a definitive diagnosis[1]; others in this group had hyperactive bladders and responded well to antispasmodics[7]; and a few may have had subclinical neurogenic bladders as suggested by Dorfman et al.[8]

Pitfalls Dependent On Bladder Size

Pitfalls for our pediatric patients with urologic problems are in part dependent on their bladder size.

Neglect

Those children with bladders larger than average will be prone to urinary tract infections and may be subject to urologic neglect if proper surveillance of their urine and proper voiding patterns are not initiated. They may also be erroneously advised that a large bladder capacity was acquired by poor training or laziness: a fact refuted by the data in this paper on children age two and less.

Eroneous Emphasis

Ignoring bladder size as a factor in females with urinary infections may lead one to overemphasis of other factors such as bladder neck or distal urethral band obstructions. Recent data from Smith[9] and Immergut[10] questioning the prevalence of those "obstructions" will help redirect attention to other factors. One of these is bladder capacity as emphasized in this study.

Lack of Parental Insight

Those children with "small bladder" symptoms of frequency, urgency to incontinence and/or enuresis may be neglected by being treated with antispasmodics or by being advised that they will "outgrow" their problems, when a thorough urologic evaluation may reveal many different pathologic conditions. The most dangerous of these are ureteral reflux and posterior urethral valves (Table 3). These children are often subjected to parental hostility for their "lack of control" or laziness. Insight into their problems will be gained only from accurate urologic data.

Summary

Bladder capacity was measured in 312 children at a standardized pressure under general anesthesia.

The average bladder size is raised in those children with infections due to inclusion of a group with unusually large bladders having a tendency to develop infections because of infrequent voiding. The increased likelihood of infections in children having oversized bladders necessitates training them to *void more frequently* and necessitates prolonging their clinical surveillance for recurrence of infection.

Oversized bladders are congenital and are not acquired through poor training or other cultural factors.

Those *children with "small bladder" symptoms seldom have a small bladder,* but usually have other urinary tract pathology amenable to specific therapy.

(Acknowledgement is made of the helpful discussions held with Dr. James Boen and Mr. Ronald Jacobson of the Department of Biostatistics, University of Minnesota.)

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See page 176 for balance of references, 3-10.

Bronchial Asthma

Treatment of the Acute Attack and Status Asthmaticus in Children

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and R. JAMES VACCARELLA, M.D.*

BRONCHIAL ASTHMA and its complications account for 12% of the medical admissions at the Childrens Hospital (4,521 of 37,481 admissions over a ten-year period ending July 31, 1970). In addition to this, many children were seen in the emergency room because of asthma.

Acute Bronchial Asthma

Emergency Room Care

The drug of choice in treating the acute asthmatic attack is aqueous epinephrine. This is given in small frequent doses subcutaneously. As a general rule, we give 0.10 ml. to a child up to 30 pounds and 0.20 ml. to a child 30 pounds or above. This is repeated in 20 minutes, and 20 minutes following the second injection, we give 0.15 to 0.20 ml. of a longer acting epinephrine, Sus-Phrine.®† The importance of the two "priming" doses of aqueous epinephrine cannot be overemphasized. Occasionally, a patient cannot tolerate epinephrine because of untoward side effects. In such cases, Bronkephrine® may be used in doses twice that of epinephrine.

If, during an observation period of 45 minutes to one hour, the patient clears completely, or to a degree that we can anticipate continued oral medications to be adequate, he is allowed to return home. It is important to instruct the mother to give either oral or rectal antiasthmatic drugs for at least 24 hours following an acute asthmatic attack requiring epinephrine. Tedral,®# Marax,®§ or similar drugs may be given orally every four to six hours, or an aminophylline suppository (Aminet®)£ every eight to twelve hours may be used rectally. Follow-up examination within this period of time is also imperative.

Intravenous aminophylline, injected very slowly over a 10-15 minute period (5 mg/kg) may be safely and effectively used in the emergency room. In the very young, it should be used with caution.

Occasionally we see a child with severe paroxymal coughing or an acute attack of dyspnea associated with hyperinflation and decreased breath sounds but no audible wheezing. These can be manifestations of asthma and, when present in a known asthmatic patient, should be treated similiar to the acute asthmatic episode, as outlined above.

If the patient does not respond to the above described series of epinephrine injections, he should be hospitalized immediately because he is either in status asthmaticus or "impending status." The response to outpatient treatment with epinephrine is the most important factor to consider in evaluating a patient for possible hospitalization. Any one or combination of the following factors can be considered critical enough to warrant in-patient care in spite of what seems to be an adequate response to epinephrine: (1) duration of the acute asthmatic episode, (2) cause and severity of previous attacks, (3) reliability of parents, (4) ability of the patient to take and retain oral medications, fluids, and nourishment, (5) presence of infection (pulmonary or extrapulmonary), (6) state of hydration, (7) ventilatory state (atelectasis?, degree of hyperinflation), (8) current or previous steroid therapy, (9) pollution or pollen index, and (10) current weather conditions, especially unstable atmospheric pressure.

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†Epinephrine suspension 1/200 dilution of which 20% is in the aqueous state (Brewer).

‡Ethylnorepinephrine HCL (Breon)

#Ephedrine, theophylline, Pentobarbital (Warner-Chilcott)

§Ephedrine, theophylline, Hydroxyzine (Roerig)

£Aminophylline, pentobarbital (Dome)

See editorial, page 135.

FOR CORRECTION SEE

Hospital Care

In a child with asthma, who is considered clinically "brittle," it is best to lean toward the side of hospitalization for observation until one is sure that he has responded to medication and has recovered from the acute episode.

The rationale for treatment is based on the pathogenic factors that contribute to the acute asthma syndrome: (1) edema of the mucous membrane of the bronchi and bronchioles, (2) hypersecretion of a thick, tenacious, viscid secretion, and (3) spasm and contraction of smooth muscle.

The treatment regimen is designed to provide bronchodilatation and adequate hydration, prevent hypoxia, and thereby prevent the development of status asthmaticus.

Bronchodilatation is maintained by small repeated doses of epinephrine as described previously. The "epinephrine series" may be given every four hours if necessary. Oral or intravenous xanthine derivitives (theophylline, aminophylline) may be used, which, because of their site of action, can augment the effectiveness of epinephrine. Occasionally isoproterenol by inhalation is used.

Adequate hydration not only helps prevent the development of acidosis but is the best method of thinning secretions and preventing further inspissated mucous in the bronchi. Often, especially in the younger age group, this can only be accomplished with intravenous fluids. Expectorants such as saturated solution of potassium iodide or glyceryl guaiacolate are of limited value.

Hypoxia is prevented by providing humidified oxygen via mask or tent. If a tent is used, care must be taken to assure adequate oxygen levels.

Infection, if present, is treated with indicated antibiotics. Appropriate cultures should be obtained before starting antibiotic therapy, but in the acute asthmatic episode, when infection is so common, antibiotics should not be withheld while awaiting culture reports. As in any organ system where there is stasis and obstruction, infection is likely. Furthermore, infection is often the cause of the acute attack or can be the main reason for the continuation of the acute episode in spite of what seems like adequate therapy.

Precautions to be followed during the acute asthmatic attack: (1) no tranquilizers or respiratory depressant sedatives should be used, (2) antihistamines should be avoided because of their atropine-like, drying effect. This tends to inspissate secretions even more and enhance the possibility of obstruction with resultant atelectasis, (3) the use of mist tents is contraindicated as this "fog" often causes further bronchoconstriction and/or increases apprehension in an already agitated child.

Status Asthmaticus

A patient is in status asthmaticus if he no longer has a bronchomotor response from epinephrine and is considered to be "epinephrine fast." Such a child is in acidosis which is one of the reasons why there is no bronchomotor response to epinephrine.[1] In children, there is metabolic acidosis due to ketonemia induced by poor caloric intake, inadequate fluid intake, and hypoxia. Dehydration contributes to thickening of the bronchial mucous secretions rendering them dry, tenacious, and viscid which causes them to inspissate and obstruct the bronchi. Edema of bronchial mucous membrane and constriction of bronchial smooth muscle add to bronchial obstruction. As a result of these factors, alveolar hypoventilation occurs with accumulation of CO_2. This increases the pCO_2 with lowering of the pH and results in respiratory acidosis. Other factors of a non-specific nature in the lungs that can play a role are areas of pneumonitis with accompanying cellular exudate in the small bronchi and bronchioles, areas of atelectasis, or even pneumomediastinum or pneumothorax.

In early status asthamticus, there are many normal ventilating alveoli as not all of the bronchial tree is involved. Also many areas of the lungs are hyperinflated resulting in decreased lung compliance. This leads to an uneven ventilation perfusion ratio in various regions of the lung. As a result, the CO_2 tension rises and the O_2 tension falls in the blood perfusing hypoventilated alveoli. However, because an increased amount of CO_2 can be removed by hyperventilation of the less affected alveoli and since the pCO_2 of "shunted" venous blood is little greater than that of arterial blood, the CO_2 tension of arteriolar blood is usually normal or below normal (hypocarbia). In contrast, similiar compensation for a low oxygen tension does not occur and hypoxemia results. As more airways become obstructed, the total volume of hyperventilation becomes insufficient to maintain a normal pCO_2 and hypercapnia occurs. Therefore, in well-estab-

lished status asthmaticus there is hypercapnia, hypoxemia, and acidosis.[2] In the early stages, because of hyperventilation of relatively unaffected alveoli, pCO_2 may be normal or low, pH may be normal, but pO_2 will be low.

Treatment of Status Asthmaticus

All patients in status asthmaticus are in respiratory distress and without exception should be admitted to the hospital, preferably into an intensive care unit.

Humidified oxygen is given immediately either by mask or tent in which there is 40-60% ambient oxygen. It should be given continuously to keep the pO_2 above 65mm. of mercury.

Arterial blood gas determinations are performed immediately including pH, pO_2 and pCO_2. Serum electrolyte determinations (sodium, potassium, CO_2 content, and chloride) and serum osmolality should also be done. If capillary blood is used for pH, the pCO_2 can be determined from the pH and CO_2 content on a nomogram. The pH, pCO_2 and PO_2 should be repeated every one and one half or two hours until approaching normal. A chest x-ray, complete blood count, and throat culture should be done as soon as possible.

Sedation can be given if the patient is very hyperactive, anxious and irritable. This should be used with great caution because of possible respiratory depression. Chloral hydrate by rectum up to 50 mg/kg will not depress respirations.

Intravenous fluids are administered beginning with a rapid infusion of a plasma volume expanding solution and then enough fluid for maintenance and correction of deficits.

Acidosis is corrected by intravenous alkalinization. Sodium bicarbonate solution is given initially. If this is not effective in a very seriously affected patient with a very high pCO_2 (above 65mm. of mercury) and a pH less than 7.2, Tromethamine Tris (hydroxymethyl) Aminomethane, (THAM)* can be used, but only if the ventilation of the patient can be adequately controlled. The amount of base or alkalinizing solution to be used can be calculated by the following formula: BE (base excess) x body weight (kg) x 0.3 = meq. alkalinizing agent. However, many patients with acute respiratory distress may have a normal base excess. It is possible then to use the Kaplan formula: dosage (in meq.) alkalinizing agent = 1.5 x body weight (kg.) per hour. The solution should be infused slowly over a period of one-half to one hour. Additional alkalinizing agent is given depending on the subsequent determination of pH and pCO_2 and the clinical state of the patient regardless of base excess. Preparations of sodium bicarbonate contain 0.9mEq/ml in a 7.5% solution. Preparations of Tromethamine Tris (hydroxymethyl) Aminomethane contain 0.3mEq. per ml in a 0.3 M solution.

The rationale for correction of arterial pH in status asthmaticus is based on improvement in systemic and coronary circulation following intravenous alkalinization and the fact that acidosis has a deleterious effect on the pulmonary perfusion in a patient with bronchoconstrictive disease. There have been instances reported in adults where intravenous sodium bicarbonate has caused prompt return of the bronchomotor activity.[3] The administration of sodium bicarbonate will generate more CO_2 and may result in a transient rise in the pCO_2 of 4-8 mm. of mercury, which is probably insignificant and takes place while correcting the pH. This rise in pCO_2 does not occur with the use of Tromethamine Tris (hydroxymethyl) Aminomethane and may be a theoretical advantage. Yet, THAM has a disadvantage in that the clinical doses employed can produce respiratory depression. Very large doses of either Tromethamine Tris (hydroxymethyl) Aminomethane or sodium bicarbonate may cause hyperosmolality because of the high solute load. Alkalinization corrects metabolic acidosis but not respiratory acidosis. Respiratory acidosis is corrected by ventilation of alveoli.

Aminophylline should be given intravenously. This is a potent bronchodilator even in the presence of acidosis. It also acts as a mild respiratory stimulant and is mildly diuretic. The dose is normally 5 mg/kg/dose, but if a considerable amount of drug has been given in the previous 24 hours, the dose should be reduced to 3-4 mg/kg/dose. Aminophylline is added to about 50cc of hydrating solution, given over a period of 10-15 minutes, and can be repeated in eight hours as needed.

Corticosteroids are given intravenously. Hydrocortisone succinate (Solucortef) should be given (by push). It is best to give two to three times the stress dose of 200 mg/m^2 per 24 hours. Give one-half of the 24 hour dose first, then follow with one-fourth of a 24 hour dose every six

*THAM-E (Abbott)

hours. The dose of corticosteroids is tapered after 24-36 hours. If the patient has been receiving maintenance corticosteroids within the past six months, corticosteroids are definitely indicated. When the patient can tolerate oral medication, Prednisone is given. If corticosteroids are given for five days or less, the drug can be stopped abruptly, otherwise gradual reduction of the dose is best. One should not expect a dramatic effect from the administration of steroids, as it takes several hours before an anti-inflammatory effect takes place.

Antibiotics should be given intravenously. This is especially important if there is evidence of pulmonary complication such as pneumonitis, atelectasis, pneumothorax, pneumomediastinum, etc. A broad spectrum antibiotic such as Ampicillin is often used.

Sodium iodide may occasionally be used intravenously to decrease the viscosity of the bronchial secretions and enhance their removal. The dosage is 25 mg. per kilo added to 250cc of intravenous fluid and given over a period of four hours, not more than once a day. If there is question of sensitivity to iodides, this drug should not be used.

At times, in spite of the above measures, the patient gets worse and develops symptoms of impending respiratory failure or the patient may be seen for the first time in this advanced state. The following clinical signs will be noted: (1) severe inspiratory retractions with gasping, (2) minimal thoracic movement with hyperinflation, (3) on auscultation of the chest, wheezing and breath sounds are barely audible which indicate a very poor prognosis, (4) depressed level of consciousness and diminished response to painful stimuli, (5) cyanosis in 40-60% ambient oxygen, and (6) the pH may be below 7.2, the pCO_2 above 65 mm. of mercury, and the pO_2 below 40 mm. of mercury. If these conditions exist, one must immediately call the anesthesiologist because measures must be taken to increase alveolar ventilation by assisted ventilation.

Intermittent positive pressure breathing with a Bennett or other comparable mechanical respirator can be attempted with a mask. A possible disadvantage is that small children won't cooperate and may become more severely hypoxic from fighting the mask. One can also try assisted ventilation with a high flow of oxygen by bag and mask, but this technique has the same disadvantage as discussed above. Isoproterenol aerosol can be used with intermittent positive pressure breathing at this time and will be discussed in a subsequent paragraph. In conjunction with these procedures simultaneous gentle manual compression of the thorax during expiration decreases the volume of trapped gas in the lungs.

The above measures are often not effective and mechanical ventilation must be instituted after insertion of an orotracheal or nasotracheal tube. This procedure should be done by the anesthesiologist and the technique commonly used is as follows: The patient is sedated with intravenous sodium pentobarbital and bagged with O_2. A short acting muscle relaxant (Succinylcholine chloride) is given intravenously. This relaxes the muscles of the thorax and abdomen permitting easier inflation of the lungs. The endotracheal tube is inserted and connected to a pressure cycled or volume controlled mechanical ventilator. The pressure cycled device provides a flow into the lung until a preset cycling pressure is achieved causing the valves to close. These devices can be triggered by the patient or self-cycled. However, decreased lung compliance and increased airway resistance may limit the volume of gas delivered with these machines. On the other hand, since the volume controlled ventilators provide the needed breath at whatever pressure is necessary to deliver the volume of air regardless of lung compliance or airway resistance, they are preferred by many.[2] With any machine, the expiratory phase is prolonged so there is slightly increased respiratory resistance preventing bronchial collapse and this provides a passive expiration. Pressures as high as 50-60cm. of water have been used to affect ventilation. After respiration is controlled, a long acting muscle relaxant, Flaxedil® (Gallamine triethiodide) is given intravenously. This drug is then continued along with sedation as needed.

Aerosol therapy can be administered through the nebulizer on the ventilator. Sterile saline is nebulized most of the time. A sympathomimetic aerosol such as isoproterenol can be used. Care must be taken in its use. The advantage in using isoproterenol is that it induces better relaxation of bronchial smooth muscle than epinephrine. One disadvantage is that after giving isoproterenol or even epinephrine, arterial pO_2 fails to rise or

even falls.[2,4] Therefore, in the presence of existing hypoxia and acidosis which in itself decreases the integrity of cardiac muscle, there is increased hypoxia. Another disadvantage is that isoproterenol causes marked increase in heart rate. Because of these disadvantages cardiac arrhythmias are prone to occur that can cause a sudden drop in blood pressure resulting in congestive heart failure. There have been reports in the literature of sudden death when epinephrine was given soon after the administration of isoproterenol.[5,6] It should be noted that since alveolar ventilation is deficient, the effectiveness of aerosolized isoproterenol is greatly reduced.

There are certain precautions we recommend in the use of isoproterenol in children in status asthmaticus. Use no more than 0.25cc of 1/200 isoproterenol solution in 9.75cc of sterile normal saline and do not nebulize this more than every six hours as needed. Nebulize with adequate oxygen. Monitor blood pressure and pulse very frequently during administration. Be prepared to digitalize by intravenous route at the first sign of fall in blood pressure or cardiac arrhythmia and increase the rate of respirations to increase oxygen administration.

Further measures of importance are: (1) endotracheal suction by strict sterile technique, (2) manual ventilation by bag with a greater pressure than that being used, for five minutes out of 30 minutes to prevent atelectasis, and frequent auscultation of the chest should be performed, (4) monitor the vital signs, pH, pCO_2, pO_2 and serum electrolytes frequently, and (5) epinephrine can be tried again after about 18-24 hours.

The patient will usually improve by 20-30 hours and by then epinephrine is usually effective. Mechanical ventilation can be stopped with the endotracheal tube in place. If respirations continue spontaneously and unlabored with good air exchange by auscultation, the tube can be removed. Endotracheal tubes have been maintained for as long as one week with no ill effects. Corticosteroids are stopped abruptly or gradually tapered after several days.

One must remember that patients with status asthmaticus should be cared for in an intensive care unit. The anesthesiologist is a very important member of the team when the patient is intubated. The nursing staff, pediatrician and allergist complete the necessary team effort in the care of these patients.

Summary

Treat the acute attack of asthma early with small frequent doses of epinephrine, maintain hydration of the patient, give adequate calories, and avoid oversedation and antihistamines. These measures can prevent status asthmaticus.

Treatment of the child in status asthmaticus should be influenced by serial arterial pH and blood gas determinations. Sufficient oxygen should be administered to restore the pO_2 to a normal or near normal level and intravenous fluids should be given to correct ketonemia and dehydration. Intravenous buffer solutions such as sodium bicarbonate should be given to correct the arterial pH, and mechanical ventilation instituted when respiratory failure is impending.

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God no such specifique poyson hath
As kills we know not how; his fiercest wrath
Hath no antipathy, but may be good
*At least for physicke, if not for food**

*John Donne: To Sir Edward Herbert at Julyers, lines 27-30.

Newborn Respiratory Distress*

A Roentgenological Approach

HUGH J. WILLIAMS, M.D.†

—Here we have a baby. It is composed of a bald head and a pair of lungs—
—Eugene Field (1850-1895) The Tribune Primer

OVER 40 DIFFERENT conditions can cause respiratory distress in the newborn infant. Clinically it is often difficult to pinpoint the exact nature of the disturbance responsible for the respiratory difficulty. Every experienced neonatologist and pediatrician has encountered infants admitted with "typical hyaline membrane disease" in whom the true cause of the respiratory distress later proved to be esophageal atresia, diaphragmatic hernia, or some other initially unsuspected condition. Definitive therapy is dependent upon a specific diagnosis and since this is often obtainable only radiographically it is essential to obtain technically good chest films without delay in every newborn infant with respiratory embarrassment. Utilizing modern high speed portable equipment, satisfactory frontal and lateral films can be readily obtained in the nursery with minimal disturbance to the infant. Any physician who has witnessed the eventual death of an infant "too ill for chest film" from a radiographically diagnosable and surgically correctible lesion such as Bochdalek hernia or tension pneumothorax will staunchly testify that the advantages of a properly performed chest examination far outweigh its risks. These conditions can be conveniently classified according to the appropriate mode of treatment into two broad categories, medical and surgical.

Causes of Newborn Respiratory Distress:

1. Medical
   1. Non-pulmonary with pulmonary manifestations.
   2. Primary pulmonary.
2. Surgical

Non-pulmonary Causes of Newborn Respiratory Distress

1. Central nervous system disease.
2. Mechanical factors.
3. Congenital heart disease.

Central Nervous System Disease

Congenital brain disorders, birth injury to the brain, intracranial hemorrhage or maternal oversedation may all result in respiratory distress secondary to diminished inspiratory efforts. In addition, a substantial percentage of infants dying from hyaline membrane disease demonstrate varying degrees of intracranial hemorrhage. This latter phenomenon is probably a manifestation of anoxia and it further burdens the overtaxed respiratory efforts of the afflicted infant. Since nearly every pulmonary condition capable of causing significant newborn respiratory distress is demonstrable radiographically, the presence of a normal chest roentgenogram in an infant with breathing difficulty should direct the physician's attention to an extrapulmonary origin. In many instances this proves to be the central nervous system.

Mechanical Factors

Alterations in the anatomical structures responsible for normal respiration may cause respiratory impairment. Respiratory distress may result from pharyngeal prolapse of the tongue in infants with significant micrognathia, such as encountered in the Pierre-Robin syndrome.‡ A large tongue, such as present in congenital hypothyroidism, may also occasionally cause airway obstruction. Alterations in the configuration of the thorax, as present in the thoracic asphyxiating syndrome of Jeune[2] or the Ellis-van Creveld syndrome£ may also cause respiratory distress in the newborn period. Hypoplasia of the thoracic cage and related musculature occurs in various congenital disorders, including the Trisomy 17-18 syndrome, and may limit thoracic expansion, thereby provoking respiratory embarrassment. Infantile polycystic kidneys may be so massive at birth that they cause compression of the lungs with resultant respiratory distress. Pulmonary hypoplasia and pneumothorax are often found in association with renal agenesis and may produce respiratory distress.

*See editorial, page 137.
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‡See page 119.
£See page 116.

Congenital Heart Disease

There are several types of inoperable congenital heart diseases characterized by heart failure, respiratory distress, and death within the first few days of life. The most commonly encountered heart disorder responsible for this sequence of events is the hypoplastic left heart syndrome. Early and accurate diagnosis is essential in order to differentiate the operable from the inoperable types of cardiac disease.

Pulmonary Causes of Newborn Respiratory Distress

1. Atelectasis
2. Hyaline membrane disease
3. Aspiration syndrome
4. Transient respiratory distress of the newborn
5. Infectious pneumonitis
6. Pulmonary hemorrhage
7. Congenital pulmonary lymphangiectasia

Atelectasis

The full-term, healthy infant completely inflates his lungs with the first few breaths of life[3] and persistent fetal atelectasis is rare. Incomplete expansion of the lungs, however, may occur in infants who are permature or possess poor musculature. Diminished aeration may also be encountered in infants with central nervous system disease or those born of overly sedated mothers. If an infant with one of the preceding disorders survives the primary process responsible for incomplete pulmonary expansion, the abnormal pulmonary densities visible on the initial chest roentgenograms disappear within a few days. Massive pulmonary atelectasis secondary to intrinsic or extrinsic bronchial obstruction may occur in the neonate and be difficult to distinguish from pulmonary agenesis. If thoracic vertebral anomalies are present, however, the most likely cause or failure of aeration of an entire lung is pulmonary agenesis since these anomalies are commonly associated.

Hyaline Membrane Disease

The respiratory distress syndrome is a major cause of neonatal death and is commonly encountered in premature infants, Caesarian section infants, and infants born of diabetic mothers. There are approximately 300,000 premature infants born each year in the United States and about 15 percent die, producing a total of approximately 22,000 deaths annually from this disease. Hyaline membrane disease may also occur in full-term infants but the incidence is low (1:6000). The etiology of this disorder is uncertain, but a deficiency of surfactin, a decrease in serum fibrinolysin, and pulmonary hypoperfusion have all been cited as possible causes[4]. Diffuse alveolar atelectasis and the formation of cosinophilic hyaline membranes in the alveolar ducts and alveoli constitute the pathological hallmarks of hyaline membrane disease. These membranes are not specific for this disorder, and similar membranes have been reported in the alveoli of older patients suffering from noxious gas inhalation, viral pneumonitis, rheumatic pneumonitis, or prolonged exposure to high concentrations of oxygen.

Most infants with hyaline membrane disease develop respiratory distress shortly after birth and the impression of a symptom-free interval of hours following delivery is usually due to inadequate observation. It can be stated with certainty that any infant who has breathed normally in all respects for eight hours will not develop hyaline membrane disease. Radiologically, a chest film taken at three hours of age will often show a fine reticulotgranular pattern in the lungs, even though the clinical findings may be mild or absent. A chest roentgenogram taken at six hours of age is nearly always positive in this disease. As previously stressed, whenever the chest film of an



Fig. 1—The characteristic diffuse bilateral reticulogranular infiltrate and air bronchogram of hyaline membrane disease were present in this 24-hour-old premature infant with this disorder.

infant with significant respiratory distress is negative, another cause for the distress, such as a central nervous system disorder should be sought[5]. The characteristic roentgenological findings of hyaline membrane disease consist of uniform, minute, reticulotgranular densities throughout both lungs (Figure 1). The tiny punctate densities represent atelectatic alveoli and contrast sharply with the air-distended brochial tree, producing the characteristic air bronchogram. In general, the more severe the roentgenologic findings in this disease, the poorer is the prognosis, particularly if the radiographic picture is progressive. Pneumothorax and pneumomediastinum are common complications and may necessitate surgical intervention. Intensive treatment, including the use of mechanical respirators, has improved the prognosis in this disease, but some of the survivors develop a therapeutic complication known as the respirator lung syndrome. Long-term studies to elucidate the eventual status of infants who develop this chronic complication are in progress.

Aspiration Syndrome

In the presence of fetal hypoxia, vagal stimulation occurs with resultant expulsion of meconium into the amniotic fluid. Aspiration by the fetus of this meconium-containing amniotic fluid produces an irregular type of mechanical obstruction in the smaller bronchi and numerous segmental areas of atelectasis. In addition to its mechanical effects, the aspirated meconium may provoke a severe chemical type of pneumonitis. Affected infants are usually postmature and demonstrate respiratory distress at the time of delivery or shortly thereafter. The roentgenologic findings are similar to those found in interstitial pneumonitis and are readily differentiated from the fine reticular pattern of hyaline membrane disease (Figure 2). There are coarse infiltrates in both lungs with associated air-trapping and diaphragmatic depression. Approximately 20 percent of affected infants die, with most deaths occurring in the first 24 hours of life. Treatment is supportive and consists of pulmonary lavage, aspiration of the stomach to remove swallowed meconium, administration of oxygen and employment of other necessary measures.

Transient Respiratory Distress of the Newborn

In most healthy infants the fluid which fills the alveoli during fetal life disappears into the pulmonary circulation with the first few breaths of life. The exact mechanism of this fluid transport into the pulmonary circulation is uncertain, but its rapid resorption is probably chiefly through the lymphatic channels and to a lesser degree of capillaries. In some infants there is delayed disappearance of this fluid, producing varying degrees of tachypnea and respiratory distress ("wet lung" disease) usually commencing within a few hours after birth[7]. Roentgenologically the lungs appear edematous and there are radiating linear streaks extending peripherally from each hilus. The presence of lung over-expansion and the fluid in the fissures aid in differentiating this condition from hyaline membrane disease, but positive radiologic differentiation is sometimes difficult on the initial chest film. Both the clinical and radiographic findings usually disappear within the first three days of life.

Infection Pneumonitis

Intrauterine pneumonitis may result from prolonged labor, premature rupture of the membranes, or hematogenous spread from an infected placenta[8]. In addition, certain viruses including rubella and cytomegalic inclusion, can pass the placental barrier and infect the fetus. Affected infants are



Fig. 2—A course infiltrate was present in the right lung of this full-term infant with meconium aspiration syndrome secondary to fetal hypoxia. The umbilical cord was twisted around the neck twice. Note the hyperaeration of both lungs due to obstruction of the smaller bronchi by meconium plugs.

usually quite ill at birth or shortly thereafter, and exhibit severe respiratory distress. Fever and leucocytosis are often absent, particularly in premature infants. The radiologic findings are those of an interstitial pneumonitis and are very similar to those of the aspiration syndrome. Clinical history, therefore, is essential in differentiating between those two conditions.

Pulmonary Hemorrhage

Pulmonary hemorrhage may occur as an isolated entity, or in association with hyaline membrane disease, the aspiration syndrome or other conditions[9]. The extravasation of red cells into the alveoli results from capillary damage by anoxia. Intrapulmonary hemorrhage is characterized clinically by the expectoration of bloody, frothy sputum. The radiographic findings are not diagnostic and consist of numerous non-specific areas of consolidation, the extent dependent upon the amount of hemorrhage. The outcome varies with the severity of the hemorrhage and the presence or absence of associated pulmonary disease.

Congenital Pulmonary Lymphangiectasia

This rare condition affects chiefly full-term infants and results from a failure of linkage of the pulmonary lymphatic spaces during fetal life[10]. Respiratory distress and cyanosis are usually present at birth and death nearly always occurs within a few hours or days. The diffuse pulmonary infiltrate somewhat resembles that of hyaline membrane, disease or anomalous infradiaphragmatic pulmonary venous return but tends to be coarser.

Surgically Correctible Causes of Newborn Respiratory Distress

1. Bilateral choanal atresia
2. Extrinsic airway narrowing
3. Intrinsic airway narrowing
4. Cardiovascular abnormalities
5. Diaphragmatic disease
6. Pneumomediastinum and pneumothorax
7. Congenital lobar emphysema
8. Cystic adenomatoid malformation
9. Aspiration pneumonitis

Bilateral Choanal Atresia

The newborn infant instinctively breathes only through the nose; oropharyngeal breathing is an acquired function which normally takes several weeks to learn. Because the newborn infant is an obligate nasal breather, bilateral choanal atresia usually causes severe respiratory distress at birth or shortly thereafter. The diagnosis is established by an inability to pass a rubber catheter through each nostril. Failure to consider and diagnose this condition is responsible for an indeterminate number of tragic newborn deaths annually from asphyxia[11]. Immediate establishment of an artificial airway is lifesaving. Elective transpalatal reaction of the obstructing septa (Figure 3) is performed later.

Extrinsic Airway Narrowing

Immediate respiratory distress may result during the newborn period from extrinsic compression of the cervical trachea by neck masses such as teratoma[12], goiter, or cystic hygroma (Figure 4). Mediastinal masses such as cystic hygroma, teratoma or duplication cyst may also provoke varying degrees of respiratory embarrassment by impinging on the intrathoracic airway or the venous return to the heart.

Intrinsic Airway Narrowing

Intrinsic narrowing of the airway may result from retrodisplacement of the tongue (Pierre-Robin syndrome), nasopharyngeal masses, or sub-



Fig. 3—Bilateral choanal atresia was demonstrable roentgenologically in this newborn infant with severe respiratory distress by a failure of the opaque medium instilled into both the right nostril (upper) and the left nostril (lower) to enter the pharynx.

glottic tumors such as hemangioma. Early recognition and surgical removal of a lesion producing significant extrinsic or intrinsic airway constriction are essential to prevent death from asphyxia.

Cardiovascular Abnormalities

Numerous congenital malformations of the heart and great vessels can cause respiratory distress in the newborn period. An enlarged cardiac chamber or pulmonary artery in acyanotic congenital heart disease may compress a major bronchus producing obstructive emphysema or atelectasis[13]. A vascular ring encircling the esophagus and trachea frequently narrows these structures sufficiently to produce choking and respiratory distress, particularly during feedings[14]. Similarly, a vascular sling (ectopic left pulmonary artery) may cause respiratory embarrassment through compression of the trachea or the right main bronchus[15]. A barium esophagogram will usually detect either of these conditions and can be simply performed with little risk to the infant (Figure 5). Total anomalous infradiaphragmatic pulmonary venous return is characterized roentgenologically by a reticuloganular pattern of the lungs sec-



Fig. 5—The arrows indicate the sites of compression of the trachea anteriorly and the barium-filled esophagus posteriorly in this infant with a vascular ring (double aortic arch). The respiratory symptoms were relieved following surgical division of the ring.



Fig. 4—Severe anterior compression of the trachea with marked respiratory distress was present in this newborn infant due to a large, benign cervical teratoma. The respiratory embarrassment was immediately relieved by surgical excision of the tumor.



Fig. 6—A large left-sided Bochdalek hernia was responsible for progressive respiratory distress in this 12-hour-old infant. Note the gas containing viscera in the left hemithorax and the marked mediastinal shift to the right. The hernia was successfully repaired surgically.

ondary to pulmonary venous congestion and a normal-sized heart[16]. The reticulogranular pattern of the lungs in this condition is similar to that encountered in hyaline membrane disease but tends to be coarser. Early diagnosis of the preceding cardiovascular abnormalities is important since surgical correction of the underlying cause is often possible with subsequent relief of the respiratory distress.

Diaphragmatic Disease

Developmental defects in the diaphragm may permit intrathoracic herniation of both the solid and hollow abdominal viscera during fetal life. Progressive respiratory distress frequently develops in such infants during the first few hours of life. The most frequent site of diaphragmatic herniation is posterolaterally through the foramen of Bochdalek, more commonly on the left[17]. Progressive gaseous distention of the herniated hollow viscera develops after birth, resulting in an escalating type of respiratory distress (Figure 6). Early diagnosis and corrective surgery of diaphragmatic hernias are mandatory. The diagnosis is often apparent clinically, particularly when bowel sounds are heard in the chest, but every experienced pediatrician and roentgenologist can recall instances where the initial clinical diagnosis of "hyaline membrane disease" was quickly amended to Bochdalek hernia following an admitting chest film. With modern roentgenologic techniques, there is little excuse for failure to establish an early diagnosis of diaphragmatic hernia in a newborn infant with respiratory distress on this basis. Foramen of Morgagni hernia and esophageal hiatal hernia occur less commonly and are seldom life-threatening. Eventration of the diaphragm, particularly when associated with other pulmonary disease, causes respiratory distress during the neonatal period and requires surgical correction.

Pneumomediastinum and Pneumothorax

Pneumomediastinum is usually secondary to alveolar rupture from increased intra-alveolar tension[18]. The antecedent alveolar hypertension may be primary from the increased respiratory efforts of a pulmonary disorder such as hyaline membrane disease, or may be secondary to the overenergetic use of mouth to-mouth resuscitation or positive-pressure apparatus. In infants, the mediastinal air progressively accumulates within the mediastinum, and seldom decompresses into the cervical soft tissues, as it does in older children and adults. If the pressure of the accumulated mediastinal air becomes excessive, impairment of the venous return to the heart may result. In some cases of pneumomediastinum rupture of the pleura with resultant pneumothorax may occur. Pneumothorax should always be suspected in any infant with mild-to-moderate respiratory distress whose symptoms suddenly become worse. Such a change should always prompt an immediate chest film (Figure 7), since an unrecognized and untreated tension pneumothorax may cause rapid deterioration and death. Needle aspiration of any significant pneumothorax or pneumomediastinum, followed by insertion of a suction, is easy to perform and is life-saving.



Fig. 7—The respiratory distress in this infant with hyaline membrane disease became suddenly worse. An immediate chest film revealed development of an acute right tension pneumothorax. The severe distress was relieved following insertion of a pleural tube and institution of suction.

Congenital Lobar Emphysema

This uncommon cause of respiratory distress, tends to involve the upper lobes and the right middle lobe. It seldom causes respiratory distress in the first few days of life but occasionally it may pursue a fulminating course characterized clinically by dyspnea and cyanosis during this period[19]. The emphysematous lobe produces com-

pression atelectasis of the uninvolved lung, depression of the ipsilateral diaphragm, and displacement of the mediastinum to the opposite side (Figure 8). Immediate surgical resection of the involved lobe is life-saving.

Cystic Adenomatoid Malformation

This rare congenital anomaly represents a hamartomatous cystic overgrowth of the normal lung respiratory elements[20]. In most instances the pathologically involved lung does not cause symptoms in the first few days of life, but sometimes respiratory distress begins during this period. This entity usually involves only one lobe, but occasionally an entire lung or both lungs may be affected. Radiologically an intrapulmonary cystic mass is demonstrable, and frequently the enlarged lobe herniates towards the opposite side. In a few instances cystic adenomatoid malformation has been mistaken for diaphragmatic hernia, owing to the resemblance of the cystic structures to intrathoracic bowel. This error can be prevented by noting that the gas-containing abdominal viscera are normally located within the abdomen in cystic adenomatoid malformation. Treatment consists of surgical resection of the affected lobe.

Gastrointestinal Tract Abnormalities

Severe anatomical abnormalities of the gastrointestinal tract often result in esophageal overfilling and tracheal aspiration with secondary pneumonitis: a sequence of events usually due to an obstructive lesion, such as esophageal atresia



Fig. 8—Lobar emphysema of the left-upper lobe was responsible for increasing respiratory difficulty in this infant. Note the compression atelectasis of the left-lower obe and the mediastinal shift to the right caused by the markedly hyperinflated left-upper lobe.



Fig. 9—Both right-upper lobe atelectasis and aspiration pneumonitis were present in this 12-hour-old infant with esophageal atresia and tracheoesophageal fistula. The admitting diagnosis was hyaline membrane disease and it was this roentgenogram which led to establishment of the correct diagnosis.

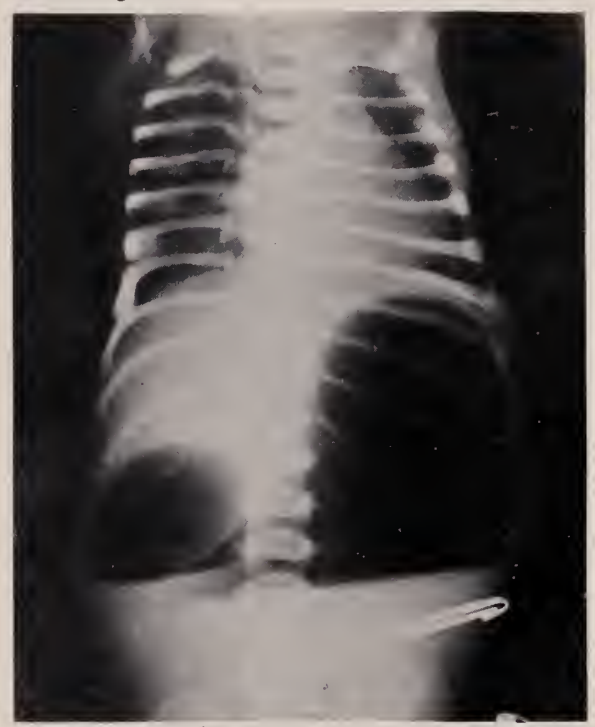


Fig. 9—Both right-upper lobe atelectasis and aspiration the right lung of this newborn infant. Note the "double bubble" configuration of the gas and fluid with the stomach and duodenum. This radiographic feature associated with a complete absence of small bowel gas is characteristic of duodenal atresia (present in this patient) or annular pancreas.

(1:5000 births). Right-upper lobe pneumonitis nearly always develops within 24 hours after birth in infants with esophageal atresia, unless preventive measures are taken (Figure 9). Aspiration pneumonitis in the newborn period may also result from duodenal atresia, annular pancreas, or small bowl obstruction from various causes. In addition, pharyngo-esophageal incoordination, chalasia and esophageal hiatal hernia may also produce aspiration pneumonitis. Less frequently, aspiration pneumonitis may result from an abnormal communication such as laryngotracheoesophageal cleft[21], biliary-bronchial fistula or jejuno-bronchial fistula.

Summary

A wide spectrum of medical and surgical disorders capable of producing respiratory distress in the newborn period has been presented. It is emphasized that the clinical signs and symptoms are similar in many of these conditions and that a definitive diagnosis can frequently be established only by a chest roentgenogram. This examination is the single most valuable diagnostic measure available in determining the cause of newborn respiratory distress. It is unjustifiable to delay radiographic examination of the newborn infant with severe respiratory distress on the assumption that he is "too sick to be x rayed." With modern equipment this valuable procedure can be performed with minimal disturbance and risk to the infant. A plea is made for the early, careful roentgenological examination of any newborn infant with respiratory distress; the potential rewards of this examination far outweigh any risk.

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Ellis-van Creveld Syndrome*

This syndrome is characterized by chondrodysplasia, ectodermal dysplasia, polydactyly, and congenital heart disease. It is considered to be a recessive, inherited defect without sex linkage. The proximal segments of the limbs tend to be more reduced in length than the distal portions. There may be super-numerary digits. There is usually no mental abnoramility associated.

*See page 109.

Durham, Robert H—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

Fractures of the Tibial Spine in Children

Open or Closed Treatment?

IVAN SCHLOFF, M.D. AND RONALD M. LAMPERT, M.D.

FRACTURES OF THE TIBIAL spine are predominantly injuries of youth, although they may occur at any age. This injury may occur independent of other injuries and is generally considered to be due to a direct blow to the anterior aspect of the flexed knee which drives the femur backwards on the fixed tibia. A rapid hemarthrosis develops, which when aspirated often contains fat droplets. It is felt that because of the relative resilient nature of the anterior cruciate ligament, trauma results in fracture of the tibial spine rather than rupture of this ligament. In a young child, hyperextension of the knee alone may be sufficient to avulse the attachment of the anterior cruciate ligament. Adults with findings of internal derangement of the knee, including abnormal anteroposterior mobility due to a ruptured or attenuated anterior cruciate ligament, sometimes demonstrate radiographically an old, unreduced fracture of the tibial spine sustained during childhood. In the very young child, the symptoms are similar to those of a torn semilunar cartilage with locking and inability to fully extend the knee. Avulsion of the anterior cruciate ligament usually occurs in children between six and twelve years of age while osteochondral fracture of the articular surface is usually encountered at a later age. In a series reported by McLaughlin of 42 such injuries 21 patients were under seventeen years of age and 21 patients were over this age.[1]

At times, the patient does not visit the doctor for several days and by this time the knee is often quite swollen. Passive extension is absent on physical examination and roentgenograms demonstrate a small flake of bone avulsed from the tibia.

Prompt recognition of this injury is of great importance. The ideal, early treatment is replacement of the displaced fragment. Closed methods are occasionally successful and should always be attempted. More often, however, the fragment must be fixed by open reduction. The best results with the closed method are obtained in children, and adults often require open reduction. Closed reduction is most successful when the cartilage is intact posteriorly and the surface area of the fragment extends under the femoral condyle so as to be compressed in extension. If conservative therapy is elected, the patient is given a general anesthetic, the knee first being aspirated in order to obtain full extension. A long leg plaster cast is then applied and immobilization carried out for a period of six to eight weeks. When the fracture is neglected for several weeks, conservative treat-



Fig. 1A—The avulsed tibial spine fragment (arrow) is visible in the anteroposterior film of this twelve-year-old boy (Case 1).



Fig. 1B—Lateral film of avulsed tibial spine fragment (arrow) (Case 1).



Fig. 1C—The avulsed tibial spine has been surgically replaced and fixed in normal position by a wire.



Fig. 2A—The avulsed tibial spine (arrow) is located in the intercondylar region of the femur in this ten-year-old girl who fell from her bicycle.



Fig 2B—The post-operative roentgenogram demonstrates wire fixation of the tibial spine in normal position.

ment is indicated if the fragment is not grossly displaced. This consists of a long leg plaster cast applied with the knee in ten degrees of flexion for a period of three to four weeks. Results, according to Blount are good.[2] Surgery is indicated whenever closed reduction fails, the fragment causes a bony block to full extension, or when the fragment is so small it cannot be reduced by manipulation. When this occurs, there is a relative lengthening of the ligament which will not permit normal function of the knee. Open reduction consists of opening the joint and replacement of the bony fragment in its bed. Using two drill holes, the fragment is fixed by inserting wires through the holes and attaching them to the tibia just proximal to the tibial tuberosity. Care must be taken not to damage the epiphyseal cartilage which is located distal and posterior to the drill holes.

Case Reports

Case 1

This 12-year-old boy was admitted to St. Paul Childrens Hospital following an injury incurred while jumping hurdles. He missed a hurdle, striking the front of his left leg. Figures 1A and 1B show an avulsion fracture of the anterior tibial spine (arrow) along with a portion of the tibial plateau. The avulsed fragment has been displaced into the intercondylar notch. Under general anesthetic the knee was aspirated and an unsuccessful attempt at closed reduction was made. The knee was then opened and closed reduction performed successfully. Reduction of the fracture fragment and internal fixation by a wire loop is demonstrated in the post-operative roentgenogram (Figure 1C). A posterior molded plaster splint was applied for six weeks.

Case 2

This ten-year-old girl was seen at Childrens Hospital following a fall from a bicycle. She struck her upper tibia on the curb, forcing the tibia backward on the femur. X rays demonstrated an avulsion of the anterior tibial spine (arrow) with displacement of this structure into the intercondylar notch. (Figure 2A) Under general anesthetic, a closed reduction was attempted, but this was unsuccessful. The knee therefore was opened and reduced as shown in Figure 2B.

Both of these patients went on to full recovery. Subsequent examinations demonstrated a full range of motion in the involved knee and stability of the cruciate ligaments.

Summary

Fractures of the tibial spine in children can result from either a direct blow to the anterior aspect of the flexed knee or from hyperextension of the knee. Closed reduction should always be attempted initially in an effort to obtain anatomical reduction. If this proves unsuccessful, open reduction should be performed in order to prevent a lengthening of the anterior cruciate ligament with resultant malfunction of the knee.

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Pierre-Robin Syndrome

The many features of the Pierre-Robin syndrome include hypoplasia of the mandible, cleft palate, retraction or prolapse of the abnormally small tongue. These cause dyspnea, cyanosis and difficulty in swallowing, aggravated when the infant lies on his back or during feeding. There is a tendency to infection, poor nutrition, and often final cachexia.

With proper treatment the abnormality improves spontaneously at the age of one month. Syphilis, alcoholic excess in either parent, avitaminosis B_2 have been considered as possible etiologic factors.

*See page 109.

Durham, Robert H—Encyclopedia of Medical Syndrome
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Pancytopenia Following Hepatitis

RAJ DUTT, M.D.* AND KRISHNA M. SAXENA, M.D.*

APLASTIC ANEMIA with or without associated pancytopenia is rather uncommon in childhood. A bone marrow aplasia can be produced by a variety of causes including genetic disorders, radiation, drugs and chemicals, infections and malignancy. In recent years the association of aplastic anemia with hepatitis has been observed in a number of cases.[1] The following report deals with a child in whom pancytopenia developed during an attack of infectious hepatitis.

Case Report

A three-year-old white female child was admitted to The Childrens Hospital, St. Paul, with generalized purpura, hepatosplenomegaly and scleral icterus.

The child had been in excellent health until about two weeks before admisison when the mother first noticed some "red spots" on both legs. The child had no fever or abdominal pain; she was eating well and was active. However, she had felt more tired for about two weeks before admission. There was no history of ingestion of any toxic substance and no exposure to any infectious disease, including infectious hepatitis.

Physical Findings

The physical examination revealed a cooperative three-year-old with a temperature of 99.4°, pulse 100/min., respirations 22/min. and blood pressure of 90/50 mm. Hg. Her weight was 35 lb. and her height was 39½", putting her in the 50th percentile for age. She had multiple petechae and areas of ecchymosis all over her body including the buccal mucosa. There was a sub-conjunctival hemorrhage in the left eye. Her sclerae were icteric but the skin was not jaundiced. The anterior and posterior cervical glands were enlarged bilaterally; non-tender, firm and freely movable. The liver was firm, non-tender and enlarged to 8 cm. below the costal margin. The spleen tip was palpable. The systemic examination was otherwise negative; the central nervous system was unremarkable.

Laboratory Studies

The initial laboratory findings were as follows: Hb 8.9 Gm%, hematocrit 26%, total WBC 3,800/ccm, reticulocyte count 2.1%, serum bilirubin 4.7 mg% (direct 3.3 mg%), alkaline phosphatase 52.3 KA unit, SGOT 1750 units and LDH—200 units with significant increase in fraction 5 suggesting liver damage. The blood was negative for Australian antigen. Platelet count was 20,000/cmm., PTT—75.4 seconds with a control of 83.3 seconds and prothrombin time 11.9 seconds with control of 11.8 seconds.

Results of some of the other tests done over the next few days were as follows: Coombs'—negative, L.E. test neg., FANA neg., infectious mononucleosis screening test neg., Haptoglobins 128 mg%, serum iron 303 mcg%, iron-binding capacity 613 mcg%, Ceruloplasmin normal, serum Folate 7 $\mu\mu$g/ml. Vit. B_{12} 590 $\mu\mu$g/ml; immunoglobulins: IgG 980 mg%, IgA 128 mg% & IgM 180 mg%. Radiographs of the long bones and chest were negative, I.V.P. was negative.

The peripheral blood film showed a severe anemia, leukopenia and thrombocytopenia. The red cells revealed hypochromia and anisocytosis, poikilocytosis, occasional target forms and slight polychromasia. Platelets were almost non-existent.

Bone Marrow

The bone marrow showed hypoplasia of all elements and fatty infiltration. There was almost complete absence of megakaryocytes and RBC precursors. There were only 2% normoblasts. The number of lymphocytes, histiocytes and macrophages was increased. Neutrophils and precursors were markedly decreased in number. Eosinophils and precursors were scarce (Figure 1).

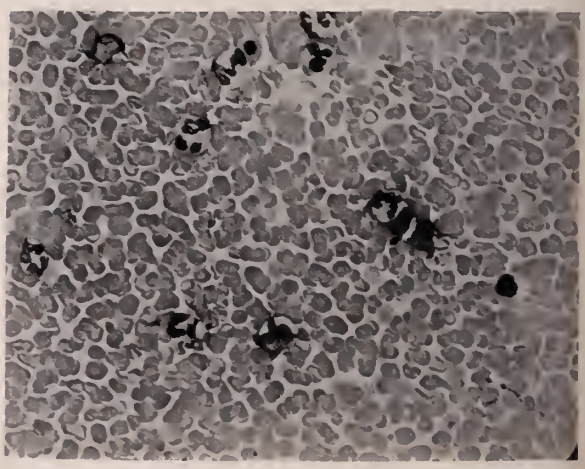


Fig. 1—Bone marrow. Note the marked hypocellularity of precursor cells.

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Liver Biopsy

A liver biopsy was performed on the eighth day of admission after a platelet transfusion. The biopsy showed disorganization of the lobular structure of the liver. The parenchymal cells were swollen and pale with a ground-glass or granular appearance and micro-vacuolization. There was some mononuclear cell infiltration around the portal spaces. It was, thus, consistent with the diagnosis of infectious hepatitis (Figure 2).

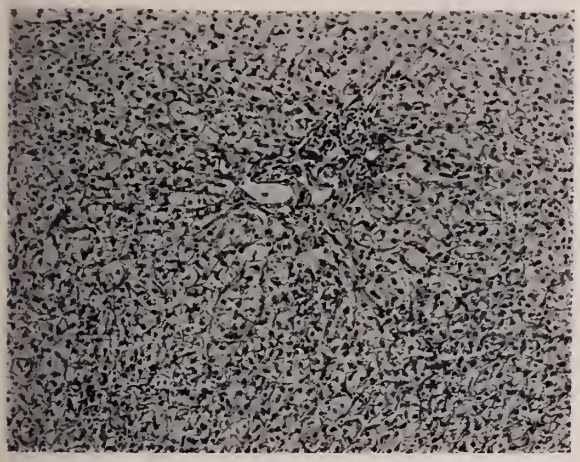


Fig. 2—Liver biopsy showing periportal mononuclear infiltration and swelling of the parenchymal cells.

Diagnosis

A diagnosis of pancytopenia associated with hepatitis was made.

Progress

She was started on Prednisone 40 mg. daily. On the fourth day of admission, she developed hematuria and blood-stained sputum. The Hb was 7.8 gm/%, total WBC 3850/cmm, the platelets 21,000/cmm. She was transfused with platelets, after which platelet count increased to 108,000. Two days later, the platelet count was again down to 42,000. The RBC, platelet and WBC changes are depicted in Figure 3 and the temperature chart and therapy in Figure 4.

On the 16th day of admission, the Hb was 5.6 gm% and the platelet count 11,000. The liver function tests done at this time showed significant improvement. On the 25th day of admission, she developed a temperature

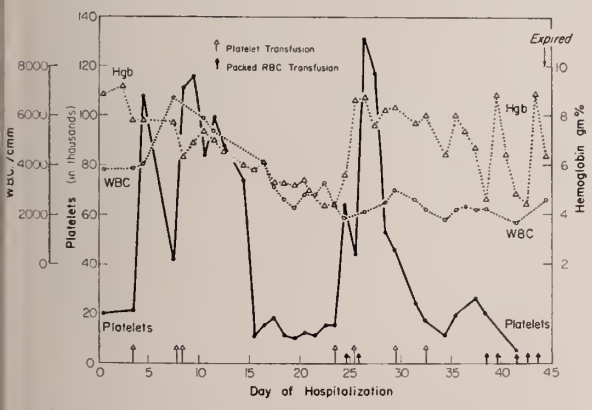


Fig. 3—Peripheral blood count and transfusions during hospitalization.

of 103°F. Blood cultures were obtained and she was treated with Ampicillin, 200 mg/kg/d and Methicillin 200 mg/kg/d for one week. The cultures were negative.

During the next few days, her condition remained unchanged. She continued to have episodes of bleeding from the gums, melena and hematuria. She was given multiple platelet transfusions to control bleeding, but it was soon evident that the platelets were being destroyed almost immediately after the transfusions (Figure 3) which were, therefore, discontinued.

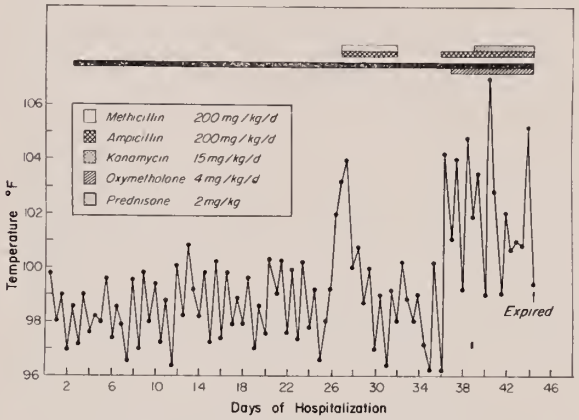


Fig. 4—Hospital course and therapy.

Her general condition gradually worsened. She became very irritable and lethargic and developed side effects of steroid therapy. Her hemoglobin continued to drop and she was transfused with packed cells with moderate increase in hemoglobin.

On the 36th day, her temperature spiked again and after cultures were obtained, she was started on Ampicillin 200 mg/kg/d intravenously but spikes of temperature ranging between 100-105°F. continued. The initial urine, blood and throat cultures were negative. However, three days later a blood culture grew E. Aerogenes resistant to Ampicillin but sensitive to Kanamycin which was started in a dose of 15 mg/kg/day. Her general condition continued to be poor although she was still alert. She developed large areas of ecchymosis all over her body and fresh blood in her stools.

The liver functions had returned to normal by this time and, since her anemia was not responding to Prednisone, it was decided to treat her with androgens. Oxymetholone was started in a dose of 5 mg/kg orally on the 37th day after admission.

On January 21, the 45th day of admission, she developed convulsions and became comatose. The cerebrospinal fluid was cloudy and smear showed gram-negative rods. The culture was positive for Klebsiella pneumoniae. She continued to have convulsions, developed shock with marked ecchymoses and melena and expired the same day. Unfortunately, permission for autopsy was refused by the parents.

Discussion

The association of viral hepatitis and bone-marrow aplasia is undoubtedly rare[1-15] and only 33 case reports have been published, to our

knowledge, in the world literature since the first report by Lorenz and Quaisar in 1955.[2] The occurrence of transient hemolytic anemia and mild transient leukopenia and thrombocytopenia with viral hepatitis is well known.[16-17] However, the patients with aplastic anemia discussed here fall in a different category. The clinical picture and autopsy findings in the reported cases are consistent enough to establish "aplastic pancytopenia following hepatitis" as a separate and definite clinical entity. The rapidly progressive course and high mortality rate of 80% make it noteworthy despite its rarity.

Initial Illness

Clinical and histological data strongly suggests that the liver disorder in these patients was infectious hepatitis. Over two-thirds of the cases were males and 50% were under the age of 16 years. The illness and initial course usually began like classical infectious hepatitis. However, in most cases, one to 10 weeks following onset of hepatitis, there was development of pancytopenia. Often the liver disorder was improving at the time bone marrow aplasia manifested itself clinically.

Our patient followed the usual pattern of presentation except that the hepatitis was mild and first became evident when the child came to the hospital for extensive ecchymosis.

Cause of Death

In 22 of the 28 cases about which we have detailed information death occurred either as a direct result of anemia and bleeding or due to sepsis secondary to neutropenia.

The survival time from onset of hepatitis ranged from three to 51 weeks with an average of about 10 weeks. On autopsy, most patients showed hepatitis in various stages of healing with evidence of massive necrosis in a few cases. The bone marrow showed hypoplasia or aplasia involving all cellular elements and replacement by fat. Evidence of bleeding and/or sepsis was present in almost all patients.

The liver condition of our patient improved but the marrow aplasia continued and she died of massive hemorrhage and sepsis. Autopsy was not permitted but the liver biopsy and two bone marrow biopsies during life left little doubt about the diagnosis.

Etiology

A number of hypotheses about the etiology of marrow aplasia have been discussed (Table).

TABLE
Etiological Factors

1. **Toxin**
2. **Auto-immune process**
3. **Virus infection:**
   Marrow depression
   Chromosomal damage
4. **Failure of liver to detoxify myelosuppressive agents**

There is no evidence that a toxin whether exogenous or endogenous is involved in the causation of marrow depression. An autoimmune theory has been suggested but not proven.[9] At the present time, it seems most likely that the virus infection itself is responsible for damaging the bone marrow. Rubella,[18] dengue fever,[19] and mumps[20] are known to produce transient bone marrow depression; marrow aplasia in cats by the virus of malignant leukopenia has been demonstrated;[12] and the MHV-3 virus[22] as well as the equine encephalitis virus[23] have produced degenerative changes in hemopoietic elements and pancytopenia in mice. Furthermore, transient mild anemia, leukopenia and thrombocytopenia occur in many patients with infectious hepatitis.[17] Thus it is not incomprehensible that during the stage of viremia more severe damage to the hemopoietic system may result in later aplasia in some patients. Another interesting possibility raised by Rubin and colleagues[1] is that the virus may cause marrow depression not by direct damage but by inducing chromosomal changes in the hemopoietic tissue. In any case, the association of hepatitis and marrow aplasia is too definite to be considered just a coincidence.

Therapy

The therapy of aplastic anemia and the support of the patient until the treatment becomes effective merit some comment. The action of androgens is slow and it may take several months before the effects are visible.[24] In our case, the institution of androgen therapy was delayed because of the presence of hepatic dysfunction. Hepatic damage has been observed during therapy with androgens.[25] In retrospect, we feel it might have been justifiable to start androgen therapy earlier.

The difficulty in maintaining respectable levels of circulating platelets by repeated *platelet transfusions* from random donors is obvious. We had no facilities for platelet matching; however, if platelets from family donors matched for histocompatibility can be given, it is possible to produce excellent clinical response for prolonged

periods of time.[26]

Another form of therapy which to our knowledge has not been tried in this group of patients but may have potential, is hepatitis *immune globulin*. It might prevent damage to the hemopoietic tissue by interfering with the virus. Whether it proves successful is still to be seen.

Summary

We have presented the case of a three-year-old girl who developed jaundice and hepatosplenomegaly with simultaneous purpura and ecchymoses. Liver biopsy was consistent with viral hepatitis. She developed a severe persistent pancytopenia and ultimately expired due to hemorrhage and sepsis seven weeks after the onset of the first symptoms. The entity of aplastic pancytopenia following hepatitis seems to be well defined and carries a very high mortality.

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Lead Poisoning in Children

The U.S. Public Health Service recommends that screening programs for the detection, treatment, and prevention of lead poisoning in children include all those children who are one to six years of age and living in old, poorly maintained houses. Lead-based paint was commonly used for home interiors as well as for exteriors until the 1940s. It has been largely replaced by titanium-based paint. Minneapolis and St. Paul have within recent years passed ordinances specifically prohibiting the use of paint containing more than 1% of lead. Cribs and other household furniture may also have been painted and repainted with lead-based paint. The lead problem is particularly important and widespread in the slums of the cities, but may also be found in old homes throughout the state.

Children exposed to other special conditions involving lead hazards should also be screened. Recent reports indicate that pencil-chewing children may be exposed to a health hazard if a large part of the painted area of the pencil is chipped of, such as a third or more of the total surface. The paint in some pencils has been reported as high as 12% lead whereas a maximum of 1% is generally regarded as safe.

Dr. Jesse L. Steinfeld, Surgeon General of the Public Health Service, has urged that more cities establish programs to locate and treat children suffering from lead-based paint poisoning and to remove the sources of lead from their homes to prevent re-poisoning. Lead-screening studies have found elevated lead levels in 5-10% of the children tested.

The Surgeon General's statement says that a concentration of 40 micrograms or more per milliliter should be considered evidence of undue absorption of lead. The current degree of exposure to lead paint in children with such blood lead values should be determined. If local resources do not permit immediate evaluation of all such children, priority should be given to those with lead values of 50 micrograms or more.

Among children who have blood lead values of 40 to 49 micrograms, those who are one to three years old should be given top priority. This age group comprises approximately 85% of the reported cases of lead poisoning and has the highest mortality rate from the disease.

Children with levels of 80 micrograms or more should be considered unequivocal cases of lead poisoning and regarded as medical emergencies. They should be hospitalized immediately and given chelation therapy, and the source of poisoning should be promptly removed to prevent re-poisoning. The statement points out that the risk of acute lead encephalopathy in this group is great, and if this brain disorder develops at least 40% of the affected children will sustain severe and permanent brain damage. Mental retardation and, in some cases, even death can result.

Until such time as funds become available for large scale screening and childhood lead control programs, the Minnesota Department of Health will assist localized areas of "high-risk" in developing and financing limited screening and control programs. Laboratory services for blood lead analysis have been and continue to be available from the Section of Analytical Services of the State Health Department. Copies of all reports of abnormal lead levels, 40 micrograms or more, are referred to the Section of Maternal and Child Health for follow-up as to medical care as well as to the source of poisoning and its elimination.

A. B. Rosenfield, M.D.*
St. Paul, Minnesota

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Spontaneous Scrotal Rupture

From an Incarcerated Inguinal Hernia

B. G. LANNIN, M.D.*

INGUINAL HERNIA is the most commonly encountered condition requiring abdominal surgery in a pediatric hospital. The performance of inguinal herniorrhaphy is exceeded in frequency only by tonsillectomy. The actual incidence of inguinal hernia in the childhood population has been estimated to be between .8 per cent and 4.4 per cent. It may be even higher in premature infants.

The largest number are observed during the first year and, in further considering those occurring during the first year, the greatest numbers are seen during the first month, with 80 per cent having been noted by the third month. Incarceration may occur fairly commonly, but actual strangulation requiring emergency surgery[1] is rather unusual. The following case report details a complication of incarcerated inguinal hernia which has not been noted in a brief survey of the literature and pediatric surgery in text books.

Case History

This full-term male infant was born of an uncomplicated delivery and seemed to progress quite normally after birth. At two weeks of age, a "lump" in the groin was noted by the family and the baby was taken to the family physician who diagnosed a scrotal hernia. Surgery was scheduled for "after the holidays." However, the lump in the scrotum continued to increase in size until it was approximately the "size of a lemon," the hernia could always be easily reduced without any discomfort. The week prior to admission, however, it was noted that the scrotum was "purplish blue." At 5:30 A.M. on January 2, 1967, during a feeding, the child appeared to stiffen up and cry and the father noted a slit in the skin of the scrotum. A short time later bowel was noted to protrude from this defect, and the child was immediately taken to the hospital where he was examined by his family physician and then promptly transferred to childrens Hospital.

Physical examination on admission showed the child to be pale, crying constantly, and clinically in shock. Examination revealed multiple loops of small intestine protruding from the defect in the left scrotum (Figure). The blood pressure was 90 and the pulse 120. The preoperative blood chemistries were essentially negative. The child was immediately taken to surgery where it was observed that there were multiple loops of small bowel protruding through a 6 cm.-long defect in the scrotum. The testicle could be observed and appeared to be in satisfactory condition. A left-lower rectus incision was made and by traction it was possible to replace the small bowel into the peritoneal cavity until the distal ileum was encountered. At this time it was observed that the last loop of terminal ileum contained a large Meckel's diverticulum. In addition, it was apparent that the blood supply in this area was compromised. For that reason, approximately 20 cm. of terminal ileum containing the Meckel's diverticulum was resected and an anatomosis made with one row of interrupted 5-0 silk. The internal ring was then closed from within the abdomen and the defect in the mesentery closed. The defect in the scrotum was left untouched.



Figure—Multiple loops of small bowel protruding from a defect in the scrotum.

*St. Paul, Minntsota.

The abdomen was then closed with interrupted silk throughout and the child left the operating room in fairly satisfactory condition.

He did quite well for the first few days, but on the fifth postoperative day a serious bloody drainage occurred from the incision and it was apparent that a wound separation was developing. The incision was carefully strapped and this was changed at intervals. Over the next few days his general condition improved but it was apparent that a large incisional hernia had developed. However, skin eventually healed completely over this defect. He was discharged from the hospital on the thirty-fourth postoperative day, with advice to the family that he be brought to the office frequently for follow-up examinations and for incisional hernia repair at a later date. The child was subsequently admitted on February 9, 1967, with nasopharyngitis and pneumonitis. He was treated successfully with antibiotics and dismissed in eight days. At the time of his admission, the large hernial defect was again observed.

The child was re-admitted on June 6, 1968, for repair of the incisional hernia. On June 11, repair was performed, at which time multiple loops of small bowel were replaced in the peritoneal cavity and multiple adhesions were divided. The hernia defect was then carefully closed. The postoperative convalescence was quite uneventful until the ninth postoperative day when it was observed that a right inguinal hernia had suddenly developed. Because of the previous history, the child was immediately taken to surgery, and the hernia was repaired uneventfully. He was dismissed on June 24, 1968, at which time all incisions had healed satisfactorily.

He has been followed at intervals and was last examined on June 7, 1970, at which time his progress was normal and all incisions were well healed. There was no evidence of either an incisional or an inguinal hernia and both testicles could be palpated, although they were somewhat high in the scrotum.

Summary

An unusual complication from an incarcerated inguinal hernia with a successful result has been reported.

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Lydate's Decision to Become a Physician

One vacation, a wet day sent him to the small home library to hunt once more for a book which might have some freshness for him: in vain! unless, indeed, he took down a dusty row of volumes with grey-paper backs and dingy labels—the volumes of an old Cyclopaedia which he had never disturbed. It would at least be a novelty to disturb them. They were on the highest shelf, and he stood on a chair to get them down. But he opened the volume which he first took from the shelf: somehow, one is apt to read in a makeshift attitude, just where it might seem inconvenient to do so. The page he opened on was under the head of Anatomy, and the first passage that drew his eyes was on the valves of the heart. He was not much acquainted with valves of any sort, but he know that *valvae* were folding doors, and through this crevice came a sudden light startling him with his first vivid notion of finely-adjusted mechanism in the human frame. A liberal education had of course left him free to read the indecent passages in the school classics, but beyond a general sense of secrecy and obscenity in connection with his internal structure had left his imagination quite unbassed, so that for anything he knew his brains lay in small bags at his temples and he had no more thought of representing to himself how his blood circulated than how paper served instead of gold. But the moment of vocation had come, and before he got down from his chair, the world was made new to him by a presentiment of endless processes filling the vast spaces planked out of his sight by that wordy ignorance which he had supposed to be knowledge.*

*George Eliot: Middlemarch, Book II, Chapter 15, 1871-1872.



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the 3 phases of Eve



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Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1,3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

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Editorials

Pediatric Medicine

THE ARTICLES in this issue are the contributions of the staff of The Childrens Hospital of St. Paul. The history of this significant institution for the Twin Cities and the State is given in Robert Rosenthal's report (page 155).

The whole concept of children's hospitals is not new, since, as Rosenthal points out, children's hospitals have been on the medical scene elsewhere in the world for over 100 years. Nor is this concept entirely new in Minnesota where we have had an orthopedic hospital for children since 1897 (Gillette Children's Hospital).

To Dr. W. R. Ramsey belongs the honor of being named the prime mover who started the forces in St. Paul which led in 1957 to the construction of The Childrens Hospital. He is the Father of The Childrens Hospital of St. Paul.

It becomes evident reading the articles in this issue that the problems of pediatrics are not the same as those faced by practitioners in dealing exclusively with adults. The unique problems of pediatrics are concentrated in the prematures and the neonates, where even such time-honored medical practices as measuring fluid requirements by weight or by surface area go by the board (See Reynolds' article, page 97 and Anderson's editorial, page 137).

Whether or not we agree with the concept of separating the pediatrics department from general hospitals creating special institutions entirely devoted to pediatrics, it is obvious that this separation is here to stay with The Childrens Hospital in St. Paul in being and the children's hospital in Minneapolis scheduled to open its doors in a year or two.

The Board of Editors of MINNESOTA MEDICINE is pleased to present this pediatrics symposium in this issue. The pages of MINNESOTA MEDICINE are open to any institution in the state which wishes to present its case material in the form of articles, and occasionally even to the extent of taking over the entire issue as is done this month.

Even to those of us who deal exclusively with problems of a different age group, it is important to keep abreast of progress in the field of pediatrics since such advances as, for instance, fluid management may lead to change in adult medicine.

Reuben Berman, M.D.
Editor

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THERE ARE FOUR circumstances which could alter the course of human diabetes: 1. Synthesis of a human insulin for general use by diabetics, thereby eliminating the development of antibodies to beef or pork insulin; 2. Alteration of the genetic material of the diabetic individual; 3. Interference with anti-insulin systems through medication; 4. Induction in all diabetics of obsessive, compulsive behavior in following a diabetic diet, using insulin, and controlling exercise.

It is obvious that synthesis of human insulin for general use may be possible in the not too distant future; that genetic alteration and drug interference with anti-insulin systems in children is doubtful in the near future; that obsessive behavior in following diet is a utopian idea incompatible with normal existence. Therefore, for the present, we must be realistic and try to control at least some of the variables that alter control of the disease: insulin, activity, and diet.

There have been numerous studies analyzing what is meant by good control. In childhood diabetes, we strive for perfection but fall short. I call childhood diabetes "fickle diabetes" because of the great variation of activity in any one child. Absolute control is impossible. However, the proper diet is one method of obtaining relatively good control and also a better understanding of the disease by the family. The Childrens Hospital diet follows this principle.

There have been numerous diets for control of diabetes. A strict diet generally has no place in childhood unless frustration is the goal. A completely unmodified diet could be of value only if used by a very mature family. A semi-restricted diet tailored to the limits of body reserves, simple to calculate and understand, coordinated with specific insulins and a normal activity level, is a most worthwhile approach to "control." This is why The Childrens Hospital diet is a real advantage for patients. It is practical, does not impose unnecessary restrictions, and the principle of fitting the diet to the disease is used.

From a technical standpoint it is difficult to evaluate this type of diet, as there are many variables, including genetics, age differences, antibody formation, activity changes, climate differences, and personality differences. The Childrens Hospital diet is being assessed in terms of acceptance by families and the adequacy of control of the diabetes. Mrs. Miller and her staff are aware of the needs for longitudinal evaluation.

Basically, the diet does not differ from any other diabetic diet in terms of calories and percentage of carbohydrates, fat, and protein. It is different in that it is presented in terms of simple categories of food, using color combinations and chart presentations which are easy to comprehend. The diet card is pocket size and easily carried. Diet, insulin, and exercise are coordinated.

On reading Mrs. Miller's Paper,* you may be surprised at how easy it is to manage a diabetic diet. Incidentally, we are also using this diet for other clinical applications such as obesity control.

Thus one of the variables of diabetes has been made more understandable through simple communication.

Stanley A. Leonard, M.D.†
St. Paul, Minnesota

*See page 167.
†Chief of Diabetic Program, The Childrens Hospital, St. Paul.

The Role of the Neonatal Intensive Care Unit in Modern Medical Practice

THE FORMATION of units within hospitals for the intensive care of seriously ill newborn infants dates from the late 1950s. Such units began when pediatricians in general were beginning to change their "hands off" attitude toward the premature infant, and as they began to gain more understanding of the physiology of the neonatal period. The capabilities of the units have been extended as a result of advances in the technology of incubators, respirators and infant monitoring systems. In response, a new area of special interest, neonatology, has developed within pediatrics: Individuals specializing in neonatology, or neonatal medicine, are specially trained in the diagnosis and

treatment of the adaptation problems of newborn infants, and the diseases that they are prone to. In addition, such specialists understand the devices used in the treatment and monitoring of such sick infants. Perhaps the most important individuals in the proper functioning of any neonatal intensive care unit are the specially-trained nurses who know how to care for a severely ill infant, and who can evaluate the status of the infant and the progress of his disease on a minute-to-minute basis.

Data available now indicate that the neonatal mortality rate for hospitals with access to neonatal intensive care units is approximately 50% of those hospitals which do not refer infants to such units[1]. There are many neonatal abnormalities for which no treatment is effective and conversely, there are neonatal problems which do not require intensive diagnosis and care. However, there is a large intermediate group who can be clearly benefited by the skills that can be used by the physicians and nurses in an intensive care unit. It is the survival of these infants that has so dramatically altered the neonatal mortality rate data quoted above.

The Childrens Hospital of St. Paul has a new intensive care unit with a capacity of 20 newborns and four older children. It is very active and serves St. Paul and the surrounding communities in Eastern Minnesota and Western Wisconsin. In addition, the University Hospital and Hennepin County General Hospital have active neonatal units. Since such units require trained physicians and nurses, they can operate efficiently only in medical centers of at least moderate size, and are not feasible for small community hospitals. Ill newborn infants can be transported to the existing units, such as The Childrens Hospital, by specially equipped and staffed ambulances. However, their effective range is limited to 100-150 miles.

The only practical way to bring the benefits of such units to all babies born throughout Minnesota, lies in the establishment of regional neonatal intensive care units in various parts of the state outside of the Twin Cities, and in large population centers in adjoining states serving as referral centers for Minnesota residents. The establishment of such centers is well underway in Wisconsin, and is proving to be a practical solution to the problem of making such specialized medical care available to all infants born in the state. Planning is underway now through a new organization called "The Great Plains Organization for Perinatal Medicine" for establishment of other regional units in the upper Midwest so that the Wisconsin model can be extended to Minnesota, the Dakotas, Iowa and Nebraska. Such an organization will require the cooperation of Minnesota physicians, the state governments and the federal government, and will therefore not be easy to accomplish. However, it is the only logical and efficient way to extend the availability of such specialized facilities to all babies in our state.

John W. Reynolds, M.D.*
St. Paul, Minnesota

*Department of Pediatrics, University of Minnesota and Director of Neonatology, The Childrens Hospital, St. Paul.

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Good-humor makes all things tolerable.—Henry Ward Beecher

One touch of nature makes the whole world kin.—Shakespeare

Bronchial Asthma

THE ARTICLE BY Strom, Austrian, Sand, and Vaccarella* in the current issue of MINNESOTA MEDICINE is timely since all practitioners interested in chest medicine, adult and pediatric, are seeing more patients with severe asthma and status asthmaticus. More deaths are occurring in severe asthmatics. The authors have brought out the importance in the outpatient evaluation whether or not the patient can be handled effectively as an outpatient or should be admitted. These factors need to be emphasized:

1. Duration of the acute asthmatic episode. If the patient has been in an acute attack for 24 hours, chances are that he is exhausted, not coughing effectively, and dehydrated. This leads to mucous impaction syndrome, alveolar hypoventilation, and respiratory acidosis. A patient in an attack of 24 hours' duration should be admitted and monitored carefully.

2. The ability of the patient to take and retain oral medication, fluids, and nourishment.

3. State of dehydration. Hydration is most important to prevent mucous impaction. This means intravenous fluid will be necessary, up to 3 liters per day.

4. Presence of infection. Usually these are acute upper respiratory infections which precipitate the acute episode.

5. Ventilatory state and the degree of hyperinflation. One can have some idea from physical examination how well the patient is moving air. But most important is what is happening to the arterial carbon dioxide tension. If the patient in the emergency room has an elevated $PaCO_2$ with acute asthma, then this is absolutely an indication for admission and careful monitoring.

6. Current or previous steroid therapy.

7. Pollution or pollen index.

8. Current atmospheric conditions.

Oxygen therapy must be monitored closely in the patient with alveolar hypoventilation secondary to status asthma just as in the patient with alveolar hypoventilation secondary to severe emphysema. Humidified oxygen should be administered in a concentration to raise the Pa CO_2 to 60 mm. of mercury. This may be 30% or 40% oxygen.

When the patient with acute asthma becomes hyperactive, anxious, and irritable, these are signs of hypoxia and hypercapnea. Sedation is contraindicated. Under these circumstances the patient must have blood gas determinations and be considered for intubation and assisted ventilation. Alkalinization corrects metabolic acidosis but not respiratory acidosis; respiratory acidosis is corrected by adequate ventilation of alveoli as the authors have discussed.

Corticosteroids can be stopped abruptly or gradually tapered after several days provided the patient has not been on steroids prior to the acute episode. If the patient has been on corticosteroids, he must be tapered slowly to his maintenance dose whether daily or every other day.

David E. Dines, M.D.†
Rochester, Minnesota

†Department of Thoracic Disease, Mayo Clinic
*See page 104.

How dear to this heart are the scenes of my childhood,
When fond recollection presents them to view—Samuel Woodworth

---

*Youth is a blunder; manhood a struggle; old age a regret.**

*Benjamin Disraeli's: Coningsby (a novel).

Urinary Tract Infections in Children

GEIST AND ASSOCIATES* have been studying bladder problems in children, and have contributed several excellent papers pertaining to this subject. These articles have been concerned with neurogenic vesical dysfunction in children with meningomyelocele[1], interstitial cystitis in children[2], and in this issue, urinary bladder capacity in children. They reported that 20 per cent of children with urinary tract infections had an increased bladder capacity.

The subject of urinary tract infections in children has been covered quite extensively in the urological literature, but its importance should be re-emphasized. Urinary tract infections are frequently associated with neurogenic dysfunction or obstructive uropathy, and consequently, serious damage to the kidneys can occur if these underlying conditions are not detected and treated early. Often, no underlying condition can be found during urological evaluation. It is possible that infections in this circumstance are associated with unrecognizable neurogenic or obstructive lesions.

Geist and associates reported that children with large bladder capacities were susceptible to urinary tract infections, and suggested a method of managing these patients. Their method of determining bladder capacity measured distensibility of the bladder wall, and may not have correlated with bladder capacity recorded under more physiological conditions. Until bladder capacities in a large sample of normal children are known, it is possible that a large percentage of normal youngsters have increased bladder capacities. In support of Geist and associates, Lapides and others[3] recently reported recurrent urinary tract infections in women with infrequent voiding habits and large bladder capacities, but with no recognizable neurogenic or obstructive lesions. Geist and associates did not report the voiding habits of their patients.

Cox and Hinman[4] have demonstrated the importance of complete emptying of the bladder in eliminating bacteriuria and thereby preventing infection. Antibacterial factors in the bladder wall and mucosa are less well understood. It has been suggested that chronic overdistension of the bladder in infrequent voiders reduces blood flow to the bladder wall, and in some way interferes with its ability to cope with infection. The exact role of the enlarged bladder in urinary tract infections has not yet been established.

The authors point out that all children with recurrent urinary tract infections should receive a careful urological examination. The importance of this evaluation cannot be overemphasized. The complete evaluation includes a urinalysis, quantitative urine culture, renal function tests, voiding cystourethrography, intravenous urography, cystometry which includes determination of bladder capacity, urethral calibration, and cystourethroscopy. Permanent damage to the kidneys of children with recurrent urinary tract infections can be prevented or halted by early and complete urological evaluation followed by adequate treatment. Further clinical studies concerning this problem, such as those conducted by Geist and associates, are clearly indicated.

*See page 100.

†Associate Professor of Urology, University of Minnesota, Minneapolis, Minnesota.

Clyde E. Blackard, M.D.†
Minneapolis, Minnesota

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Reminder

110th Annual Meeting of the Minnesota State Medical Association in Rochester, Minnesota, May 18, 19 and 20, 1972.

Newborn Respiratory Distress: A Roentgenological Approach

In the current issue of Minnesota Medicine* Dr. Hugh J. Williams has discussed the wide spectrum of medical and surgical disorders capable of producing respiratory distress in the newborn. He has emphasized that clinical signs and symptoms are similar in many of these conditions and that a definitive diagnosis can frequently be established only by a chest roentgenogram. The most important contribution of this review of the subject of newborn respiratory distress, is not so much the necessity of a careful roentgenological examination, but rather the awareness that there are over 40 different conditions that can cause respiratory distress in the newborn. If we keep in mind when we are asked to see an infant in respiratory distress that this may be due to a tension pneumothorax or massive atelectasis and utilize the positive physical findings that should be present with radiographic and arterial blood gas support, we may correct a clinical situation with thoracentesis or bronchoscopy that might otherwise have had a fatal outcome. Positive physical findings will be present (such as decreased or absent breath sounds on one side, retraction, shift of the mediastinum, stridor, unilateral wheeze, flatness to percussion of an effusion, and diffuse rales and rhonci of aspiration—to mention a few). When the positive physical findings are correlated with the emergency chest xray and comparative chest xrays if available, we should be able to differentiate the medical and surgical disorders capable of producing acute respiratory distress and initiate appropriate treatment early. I differ with the summary that the chest roentgenogram is the most valuable diagnostic measure available in determining the cause of newborn respiratory distress. The physical examination with a knowledge of the differential diagnosis and a high index of suspicion is still the most valuable diagnostic measure. The history, physical findings, emergency chest roentgenogram, and arterial blood gases utilized together can best establish the etiology of the newborn respiratory distress.

David E. Dines, M.D.†
Rochester, Minnesota

*See page 109.
†Department of Thoracic Disease, Mayo Clinic.

Maintenance Fluid Requirements

In this journal there is an article that relates to maintenance fluid requirements, especially in prematures and other neonates.* The author, John Reynolds, writes from a rich experience with intravenous fluid therapy in tiny babies. St. Paul Childrens has pioneered neonatal intensive therapy in this part of the country and for some time has had a nationally recognized, outstanding neonatal intensive care nursery and center.

Dr. Reynolds makes the point that the basal fluid requirements are related to the body's metabolism as well as its mass. Heretofore we have been estimating fluid requirements only by measures of body mass, namely weight or surface area. Because of the prematures and neonates' unique metabolic requirements, it is critical that body metabolism be taken into account in estimating fluid requirements.

More and more teaching centers in pediatrics are including body metabolism as a factor in determining fluid requirements, and currently there is a trend in this country to estimate all children's fluid requirements on a caloric rather than a weight or surface measure.

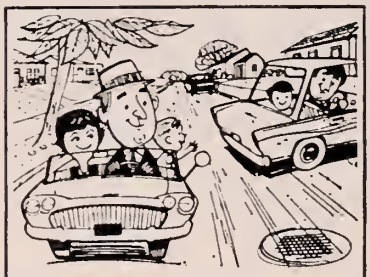
We are indebted to Reynolds for highlighting this refinement in pediatric fluid therapy sharing with us the importance for newborn infants that body metabolism be taken into account in determining fluid requirements.

Arnold S. Anderson, M.D.
Minneapolis, Minnesota

*See page 97.

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Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (i.e several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications

Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings

When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with the high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children Not recommended for use in children under 12 years of age.

Precautions

In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorectic agent and a restrictive dietary regimen.

Adverse Reactions

Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration

The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage

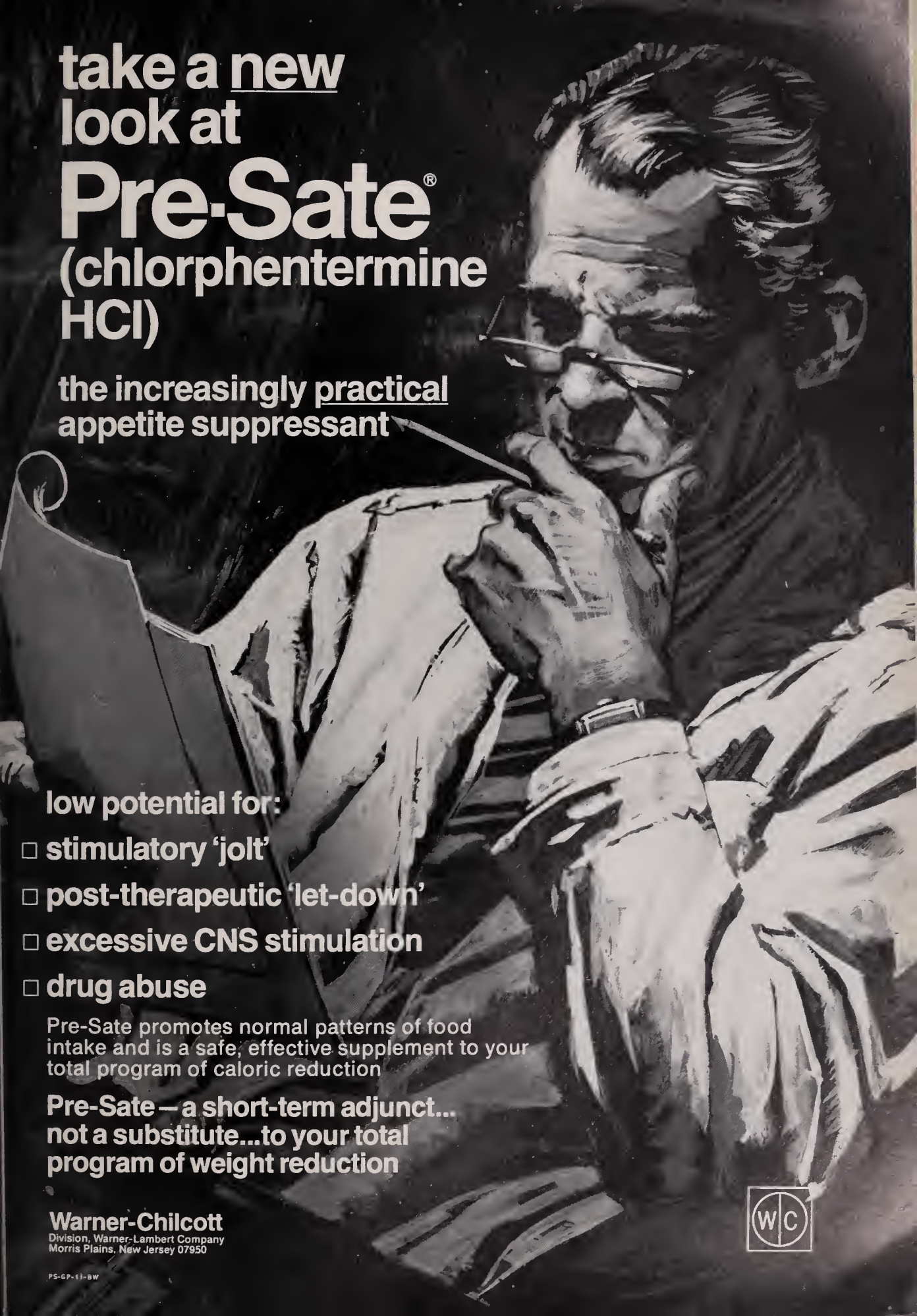
Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied

Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

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When you select this familiar antibiotic for IV infusion you have available a broad dosage range that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomycin hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in not less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25—30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

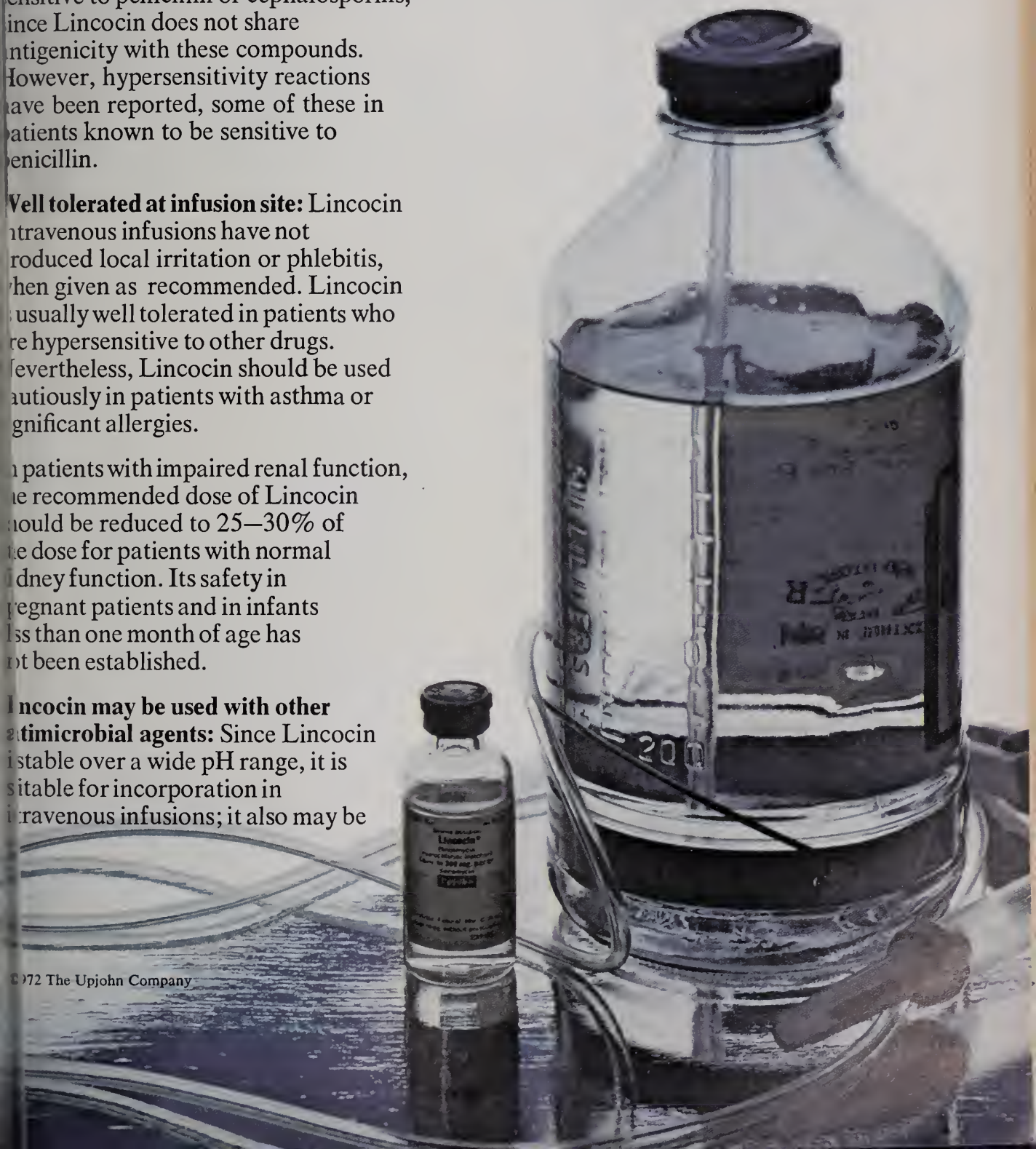
Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®
(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

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The Viewing Box

Paroxysmal Abdominal Pain in Children

ALLAN DEWALD, M.D.*

THE PATIENT, a one-year-old male, had severe abdominal pain for several hours prior to admission and two episodes of vomiting with passage of a small amount of bloody mucus by rectum. A film of the abdomen (Figure 1) indicated the presence of a soft-tissue mass partially outlined by gas in the mid-transverse colon (arrows). Several moderately gas-distended loops of terminal ileum were present.

Following this film the child became asymptomatic and fell asleep. Two hours later there was a recurrence of symptoms and a barium enema was performed. In the left transverse colon an intraluminal mass was encountered which preceded the barium column to the cecum. No barium refluxed into the terminal ileum. A post-evacuation film (Figure 2) demonstrated a mass in the ascending colon partly delineated by a coil-spring type of barium distribution.

What is your diagnosis? (See next page.)

*Rapid City, South Dakota.



Fig. 1—The admission abdominal film demonstrates a soft-tissue mass outlined by gas in the transverse colon (arrows).



Fig. 2—The post-evacuation film following barium enema demonstrates a large intraluminal mass in the ascending colon with a typical "coil spring" configuration. The appendix is filled with barium but there is no terminal ileal filling.

Diagnosis

The mass represents the head of an ileocolic intussusception which was only partially reducible by the barium enema. Surgical reduction was immediately performed. No lead point for the intussusception was demonstrable.

Discussion

Intussusception is a telescoping of one loop of bowel into another. It most commonly originates in the distal ileum and may cause mechanical small bowel obstruction. Sixty percent of intussusceptions are ileocecal, thirty percent ileocolic, with the remaining ten percent composed of ileo-ileal, ileo-ileocolic and colocolic varieties. Transient ileocolic intussusception undoubtedly occurs more frequently than is generally appreciated and probably constitutes a common cause for indeterminate intermittent abdominal pain in children.

Eighty-five percent of intussusceptions occur between six months and two years of age and is twice as frequent in males as in females. In infants and children the cause is most often idiopathic. Adenoviral infections of the intestinal tract may precipitate intussusception by causing hypertrophy of Peyer's patches and hypermotility of the gut. A lead point is demonstrable in less than two percent of infants under two years of age. Beyond this age a lead point is more commnly found, including in order of frequency, Meckel's diverticulum, polyp, lymphoma, duplication cyst and small bowel hematoma (Henoch-Schoenlein purpura, hemophilia or leukemia).

Clinically, intussusception is characterized by the sudden onset of paroxysmal abdominal pain and vomiting. During bouts of pain the child is often pale and "shocky" but becomes asymptomatic between paroxysms. Early the abdomen is stiff and hard during attacks, only to become soft and relaxed between paroxysms of pain. The soft tissue mass of the intussusception is sometimes palpable, particularly during periods of relaxation. Rectal bleeding is uncommon in early intussusception and only 50 percent will demonstrate this finding (currant jelly stool) by 24 hours. Rarely will the intussusception protrude through the rectum and simulate rectal prolapse.

The abdominal roentgenogram may be non-contributory in intussusception. Commonly, however, there is an absence of gas in the right half of the colon. The soft-tissue mass of the intussusception will be outlined by colon gas in 20 percent of patients. Gas and fluid-filled small bowel loops will be evident if significant mechanical obstruction is present. However helpful the plain films may be, the barium enema is the most definitive diagnostic procedure. It will often demonstrate the characteristic coil-spring pattern due to permeation of barium between the intussusceptum and the intussuscipiens. In addition to being diagnostic, the enema can be employed therapeutically to successfully reduce up to 80 percent of early cases. Hydrostatic reduction should not be attempted in cases with evidence of peritonitis or severe small bowel obstruction. Even if the intussusception is incompletely reduced hydrostatically, the procedure is valuable since it simplifies subsequent surgical reduction. Because a successfully reduced intussusception may recur with evacuation, a post-evacuation film should always be obtained to check for recurrence.

Discretion in speech is more than eloquence.—Bacon

Family Practice

How Do I Take Care of My New Baby, Doctor?

ALBERT G. MILLER, M.D.

TWENTY YEARS AGO this question would have worried me greatly for no one in my medical school or post graduate year took time to include this basic knowledge in my pediatric training. If this same mother had asked me how to treat her child with tuberculour meningitis, syphilis or leukemia, I could have quickly and calmly outlined the available therapy.

Today I can answer her first question with promptness and assurance, but contact with the medical students and house officer at Childrens Hospital has convinced me that their exposure to this basic pediatric problem is no better than mine a generation ago. The modern pediatrician would probably answer her question with, "Mrs. Jones, let me introduce Miss Smith, my pediatric nurse practitioner. She will answer all your questions about your new baby."

After opening a private practice with a paucity of practical knowledge, one must collect this essential learning through questioning older colleagues, by trial and error care of his own children, in reading practical literature and by growing from your patients' experiences and comments as you guide them with decreasing ignorance.

As you mature, you develop certain clinical impressions upon which you add, modify, or discard as your dialogue with mother takes form. One hesitates to put them into writing for my impressions may solve problems in my practice, but perhaps they may not withstand the critical analysis of colleagues and mentors. Yet, these answers to practical questions may help the new pediatrician gain the confidence of his mother and rapidly increase his practice.

If one organizes his daily visits to the new mother, he will not sound like a broken record repeating what he just explained to another mother on the maternity floor. He will know what he will discuss with her today, what he will tell her tomorrow, what he will tell a second new mother that same day, and so on through the mother's post partum stay in order to tell each the complete story without needless repetition and without overburdening her with too many new facts in one visit. One needs to modify his presentation for the mother who appears anxious and overwhelmed by her new situation, and needs more discussion and reassurance, but the basic dialogue remains fairly constant. (The only thing that throws me into slight panic yet is finding on the third morning that the obstitrician has promised the yet unengorged nursing primipara that she may go home today.)

The thorough, though busy, pediatrician must visit daily spending five or ten moments helping her gain confidence in herself and in turn in him. It is time well invested to enable the mother and child to go home knowing each other to a fuller degree, and there will be many fewer telephone calls at all hours frantically seeking help.

You must decide that you like this facet of pediatric practice, for when five hundred new babies enter your practice each year, a certain portion of your available office appointments need to be held open for the five or six well-baby visits required the first year of life. It can be a very gratifying experience as well as a financial asset for your practice.

In 1970 five hundred and one newborns were seen. The majority were normal infants but problems such as prematurity, multiple births, hyperbilirubinemia, hyaline membrane disease, infants of diabetic mothers, tetany, chromosome abnormalities, congested heart disease, craniosynostosis, imperforate anus, nerve palsier, sepsis, scalded skin syndrome, and minor orthopedic problems such as club feet and fractured clavicles produced a high enough incidence of pathology to keep one observant, stimulated and studying.

Two hundred thirty-nine mothers chose to nurse while 241 preferred to use a formula. An

additional 10 infants died within a few hours of birth from prematurity or severe respiratory distress, so these mothers had no opportunity to denote a feeding preference. A final 11 newborns were so premature that I chose to use a 24-calorie iron fortified formula rather than giving the mother the option to try breast feeding.

Thus, roughly, fifty percent chose to nurse their infants. Five nursing mothers did not return for follow-up care, but of the others, only ten had discontinued nursing at the one month's visit.

The decision to nurse must be made by the mother before the time of delivery. To enjoy nursing she must be enthusiastic in her decision. If her nine months of pregnancy have not given her sufficient time to decide resolutely in the affirmative, perhaps guilt feelings or family pressure are pushing her toward an unhappy choice. Give her emotional support by pointing out that her baby can grow both physically and psychologically on a par with a breast-fed infant. She can be just as much the complete, loving mother feeding him by bottle if she holds, cuddles and loves him each time.

For the mother whose joy is in nursing, enthusiastically second her decision at your first meeting, and then support her the following days when the discouragement of a sleepy baby and the discomforts from stitches and engorgement weigh heavily against her initial choice.

Advise the mother that her baby is expected to lose the next several days as he will be voiding and dirtying his diapers many times before he begins to eat enough. It may be a week or more before he gets back to his birth weight and it is possible the baby will not gain it all before he goes home.

The mother should be told the baby will be breast fed every three to four hours. If he is sleepy, a few drops of cold water on his forehead are more likely to awaken him than will pinching his cheek or slapping his bottom. She should support her breast with one hand, pulling it back from the nipple with her thumb and forefinger. This will make the breast easier to grasp and will also keep the breast away from his nose and allow him to breathe. Touching his cheek to the nipple will help him find the nipple. He should get a good mouthful of breast including part of the colored area. When he is to be removed, first break the suction by pulling his chin down or by gently prying the corner of his mouth from the breast. Just tugging him off will soon produce a sore nipple.

Let him nurse up to three minutes on each breast the first day and just four minutes the next day. This gradual start will stimulate breasts to produce milk in two or three days without letting nipples become cracked or painful. There will be no formula as he does not need the calories at this stage. The formula will decrease his urge to nurse, for the milk comes far more easily from the bottle than the breast.

Through trial and error the mother will determine how often the baby needs to be burped. If he spits up when burped after the first three minutes, do it more frequently until the baby learns to swallow less air in the succeeding days. There is no harm in not burping, although he is more apt to spit up some milk later, or perhaps he may sleep longer if he gets the air up promptly and replaces it with additional milk.

Once milk comes in the mother will be waiting for the baby to relieve the discomfort of her engorgement.

In regard to diet, unless a food upsets the mother, it is rare that it will bother the baby. There are a few foods to watch, however. In eating chocolate take a few pieces rather than eating half the box at one time. As for spicy foods, start with a small pizza instead of the king-sized one. Some people do have trouble with gassy foods, such as beans, onions, cabbage, and cauliflower, so moderation can be observed through taking only one serving a day. Drinking large amounts of milk, beer, or tea will not increase your milk supply.

Bromides pass into your milk in large amounts but barbituates do not. Sulfa may come through in harmful amount, but penicillin and other antibiotics will not. Aspirin and Darvon will cause no harm, but ergot in migraine tablets can be dangerous. The caffine in your coffee and alcohol in moderation will do no harm, but more than a few cigarettes may reduce the milk production but the nicotine will not affect the baby. If you need to take cortisones, it is recommended that one discontinue to nurse. Ordinary laxatives such as mineral oil, milk of magnesia, X-lax, and senna are safe, but cascara and Dovbane may cause trouble.[3]

Most babies are alike in having extra mucus

the first days. They rattle and gag on it and often end up regurgitating it. The mother should call the nurse and she will clean him up for you. Babies get lint up their nose and sneeze every now and then. It is the only way they can blow out the tickles and it is not the onset of a cold. Babies hiccup frequently often after each feeding. It is just a harmless jumping of his diaphragm, and a swallow or two of water often stops it. Otherwise, after several minutes they will cease by themselves.

Over the years it has become necessary to mention the sneezing and the hiccuping or the mother will raise the question sooner or later—often by telephone after getting home. If the inevitable regurgitation of mucus or colostrum is belittled before it occurs, the mother will be more completely satisfied than if the same explanation is given post facto.

Even if it is not her first baby, mention the point of individuality. Ask her to forget how her last baby ate or slept or cried for even brothers and sisters don't behave the same like peas in a pod. The only real difference is that a baby boy wets many more diapers a day than will his sister. But, any other variation in physiological responses, temperament, and activity pattern is just due to two different personalities independent of sex.

For a formula feeding, standard brand, eight-ounce, wide-mouth, pyrex bottles are recommended. The terminal method of sterilization with emphasis on the need for an adequate period of boiling (twenty-five minutes of active boiling) and the necessity of using adequately cleaned equipment should be stressed.

The first two or three bottles should be just sugar and water. Following this period the baby will be offered formula if he is awake enough to want some. After the initial twenty-four hours offer an ounce of Enfamil, and this should be increased each day. The gradual approach will give the digestive tract time to adjust. Give the baby sugar water, in addition if he indicates he wants more liquid than the formula offered.

At home start with four ounces in his bottle and let the infant take what he wants over a twenty minute period plus adding on time taken for burping. Hold the bottle at an angle that keeps the nipple full of milk. As soon as he or she can drain the whole amount, increase the bottle by one ounce the next day so as to keep one jump ahead of him. We seldom go beyond eight ounces, for by that time he will be old enough to try some solid food. Do not keep formula leftover for the next feeding. Too many bacteria will accumulate to make it unsafe.

Some vigorous babies can empty a breast in two minutes while the average infant takes four to five minutes; but most of them enjoy sucking at the empty breast for a longer period. But, after ten minutes excessive air swallowing occurs, and the probability of developing a sore, cracked nipple increases.

The baby may become quite sleepy after emptying the first breast. It is entirely possible he will be completely satisfied with just one breast. Nursing time can vary from two to five minutes on one breast up to a total of twenty minutes on both breasts.

Within reason a baby can establish his own feeding schedule, but he will have to learn to wait at least three hours from the start of one feeding to the start of the next, or the mother will be spending all her time just feeding and changing the baby. If he can sleep four hours or more, let him. In the beginning, wake him at the end of four and one half hours during the day, or too long a nap might get his days and nights reversed and have the mother up every two hours at night. Let the infant sleep as long as he will at night. As soon as he regularly sleeps at least eight hours at night, gradually lengthen out the feeding intervals during the day. Some sleep through the first night at home, while others just as normal, will be four months old before they omit the two A.M. feeding. At three months some babies are down to three feedings, while others are still nursing eight times around the clock, but 90 percent are good sleepers by that time.[5,6,7]

The mother should be relaxed at nursing time to enable the let-down reflex to occur. This reflex helps the baby get the milk. Normally, sucking causes a hormone to enter the mother's bloodstream. This acts on the tiny milk sacs in the breasts to make them squeeze the milk into the bigger ducts where it can be sucked out. Sometimes just thinking about it will start the milk letting down and dripping from the breasts. Tension, worry, and especially pain from the tender nipple can interfere with this most important reflex.[10]

(I have never found it necessary to use Syntocinon nasal spray to stimulate this reflex. If

one takes time to visit the mother, offer advice, answer her questions, and allay her fears sufficient natural hormone will be secreted to elicit a satisfactory let down.)

After feeding, a baby should be put to bed on his abdomen, so that any milk spit up will end up on the sheet and not in his lungs. A second important reason for this position is that if left sleeping on his back, he will keep his head turned to the same side the first four months. Just the weight of his head will push the soft skull bones out of shape creating a lop-sided appearance both in the back and on his forehead, with one ear edging an inch ahead of the other. Kindergarten exam time reveals that these changes in shape can be permanent.

Do not have the crib in your bedroom. His cry of hunger or wet diaper will be easily heard.

Too many covers might result in a heat rash. Start with a six-year crib right away, for the limited circulation of air in a bassinet or cradle helps promote overheating him.

At first bowel movements are thick, black and sticky, and appear during each feeding. Later they will become much looser. Most babies go on to have yellow or orange stools in a few days. But, in some infants this transitional pattern can persist two or three weeks with the stools remaining green and often being explosive. They can also contain mucus, and may occur frequently.[13]

If he grunts and groans, turns red or purple, thrashes about or even cries when his loose movement squirts out, help him by inserting a finger or a thermometer into his rectum.

The consistency of his stools can vary from hour to hour or from day to day with some being mainly water, some watery and curdy and some pasty; but it will be unlikely but not impossible that he will have a formed stool. As the days go by his stools may gradually decrease in number and there may be days with no stools at all.

The Committee on Nutrition of the American Academy of Pediatrics has recently re-emphasized it's recommendation that iron-fortified proprietary formulas be used to prevent iron-deficiency anemia of infancy. In addition, the Committee suggests it be used "as beverage milk until the infant is at least 12 months of age."[14] Except in the case of a premature birth, a baby with low birth weight, multiple births, or an infant of an anemic mother use the standard, concentrated liquid form without added iron. Each year the author finds more than one or two of his infants at the age of 12 months having a hemoglobin under 9.5 gm%. The majority have a hemoglobin value of 11.5 gm% or above. Therefore, there is no need for the added iron for the average baby. The parents have difficulty in getting their grocer or druggist to obtain the iron-fortified formula. Too frequently it takes much insistence to keep the baby on formula for four months, so it is doubtful that a mother can be convinced she should use formula for a full year. In addition there is a price factor involved with twenty-six ounces of formula costing thirty-one to thirty-three cents and a half gallon (64 oz) carton of whole milk varying from forty to forty-eight cents.

Some mothers use a proprietary formula other than Enfamil, because they used it previously or heard of it from a friend. Rarely, an older mother still prefers to use an evaporated milk formula that she made for all her older babies.

Start some vitamin C and D when he is two-weeks old. Our water contains a small amount of fluoride to help build stronger teeth, but since most breast-fed babies take little or no water a fluoride supplement is needed.[15]

Fill a plastic dropper up to the 0.6 mark, put it way back on his tongue and the baby will swallow it slowly down his throat. It can be given at any time of the day, but get in the habit of doing it at the same time each day, for developing the habit will keep you from forgetting these essential nutrients."[17] (The formula used by Mrs. Brown has an adequate supply of vitamins only when Robert drinks a full can each day. Mrs. Brown will use 0.3 cc of Trivisal to guarantee an adequate amount without excessive waste. The water used to mix the formula supplies sufficient fluoride.)

Solid food can be started at the age of one month. A baby does not need it before he is four or five months old,[18] nor does it mean he will sleep any longer, nor grow any faster.[6,7,8] At their proper time solids are needed to supply iron which is completely lacking in milk. Some babies absolutely refuse food at first, but all will accept it by the age of five months if no one has panicked and tried to force feed them.

Start with fruit either applesauce, bananas or pears rather than cereal. Feed him the fruit twice a day. Babies seem to prefer the taste (or feel) of fruit, they develop fewer allergic problems; and they seem to get less fat and overweight. Their

intestinal tracts do not supply an adequate supply of digestive enzymes from their pancreas to properly digest starches the early months of life.[19,20] Some experts feel the introduction of wheat or rye too early in life may produce diarrhea due to sensitivity to gluten.[18]

It is not necessary to specially prepare baby food which has a high cost (4¾ ounces of applesauce for 12 cents versus 50 ounces of good adult brand for 59 to 69 cents), often contains allergy-producing citrus juices or fruits and may be diluted with tapioca, noodles or flour. Combined foods do not allow one to spot what item is producing the new-rash, stomachache or diarrhea.

At ten days, start giving him a bottle at least once a week. Without experiencing an occasional bottle of formula he may stubbornly refuse it when you do wish to skip a feeding or when you decide to wean him. Offering a bottle of water is not an adequate substitute, for even if he accepts the water, he may still refuse formula. If an entire nursing is substituted, let him take what he wants during a twenty-minute feeding. The first bottle or two may be accompanied by some spitting up, until he gets used to that type of nipple.

Enfamil is one of the many good formulas manufactured to imitate breast milk. For the occasional feeding the ready-to-use bottles are a convenience; they are sterile; and they need no refrigeration. Remove the cover, screw on a standard nipple and his bottle is ready; unless the baby has become too accustomed to the warmth of breast milk and sulks until the formula is warmed. Most stores stock them in three sizes—four, six, and eight ounces. The bottles may be reused, but of course any leftover must be discarded.

Some mothers prefer to offer a bottle each evening so as to encourage their husbands to take over the 10:00 P.M. or 2:00 A.M. feeding. At that frequent use powdered formula is more economical than nursettes. If the formula is given immediately after its preparation, sterilization is not necessary. Terminal sterilization is mandatory if the formula will not be used within thirty minutes, however.

Each diaper change, both for urine and stool, calls for use of both soap and water in that area. A full bath does not need to be a daily ritual only when the need is evident whether it is twice a day or once a week. There is no scientific reason for doing it in the morning, and an evening bath may be more relaxing and sleep producing. It will also give the father a chance to bathe him. Nor does it matter whether it is done before or after a feeding.

We use a purple dye on the baby's cord. It prevents infection and delays the separation of the cord for up to three or four weeks. Tub the baby as soon as he gets home, but dry the area thoroughly after his bath. If the stump becomes sticky, you can wipe about its base firmly with cotton and alcohol three or four times a day. Do the same thing if the navel spots any blood for a day or two after the cord drops off. No belly bands or dressings need be used.

In the nursery Phisohex is used to prevent the more resistant hospital bacteria from causing skin infections. In the home environment, use ordinary soap such as Ivory or Lux, rather than the medicated soaps, such as Dial, Safeguard, Lifebuoy, Phase III, Zest, Phisohex, etc. Hexachloraphene, the halogenated salicylanilide, and similar disinfectants found in these soaps tend to dry a baby's skin after repeated use, and for some it can cause a contact dermatitis or severe skin reaction when exposed to sunshine.[21,22,23,24] Some experts feel there may be harm done in killing off the everyday bacteria on our skin, for more pathogenic bacteria or fungi may then invade and cause disease.[21,26] Ivory is more economical also.

If cradle cap develops rub some vaseline in well at bedtime, shampoo the next morning and rub out the scales with the towel or washrag. Repeat this for a few days until all the scales are gone, and then do it again in a few days, a week, or a month later when it returns. If the baby has long hair, the vaseline is too difficult to wash out, and it is necessary to use the more expensive Fostex cream shampoo or Head and Shoulders.

If winter weather or too frequent bathing leads to development of dry skin, use Nivea cream in place of oils or lotions.[27]

Baby powder or cornstarch can be used in the diaper region if a mild irritation develops. That area will remain cooler and less irritated if snap-on pants are used rather than the pull-on plastic or rubber pants.

In the summer air conditioning is used in the hospital and should be used at home for comfort if available, but a fan or a breeze through an open window can be substituted. Wind on his face does not make increased air swallowing

("gas"). It is an old wives' tale that wind on his ears causes an earache. The more he gets outside, the better he will sleep.

The first few months he has built-in protection in the form of antibodies from you, against seldom seen diseases such as diphtheria and polio, but he has no such defense against the common cold, strep throat, or the ever-present flu. A cold may not develop into anything serious, but if the small-sized nose gets plugged the baby will have difficulty in nursing and sleeping, so his fussy periods will increase in frequency and length.

If circumcised, no vaseline or dressing is needed to protect it from the diaper. Wash the penis during his bath and when you change his diapers. Soap and water will not hurt it. If the circumcision was extra short leaving a raw area on the shaft, have the mother apply vaseline there for a day or two. The average mother (or father) will not retract the swollen foreskin remnant even if directed to do so. At the six week exam any adhesions that have reformed between the corona and foreskin can be easily broken down with less trauma for the parents.

At home some babies behave miraculously for a few days and then on the fourth or fifth day spend most of their time crying. If no one gets too upset, peace usually returns the next day. A car ride will often quiet a noisy baby, for the engine vibration seems to lull him back to sleep at once. The sound of a vacuum cleaner, the hum of a radio tuned away from any station or the buzzing of an electric razor may also solve a crying situation. Occasionally, holding the side of the vibrating razor against the baby brings results when the sound alone has no effect.

A pacifier is also a handy gadget that entertains and quiets a baby if he cannot find his thumb. A nipple plugged with cotton often does better than the fancy commercial article that has a handle which catches the baby's waving hand and is repeatedly knocked from the mouth.

Don't be too anxious to start on the pill again. The hormones may make your milk supply decrease or even disappear. Nursing does not guarantee the mother she will not become pregnant again. It is unlikely that she will conceive until the baby is ten weeks old, unless she has a menstrual period before that time.[28]

The first days at home the mother will find herself tiring easily. Her milk supply will decrease somewhat for about forty-eight hours, but it will rebound again to very adequate levels. Without the nurses near, she may well become apprehensive, and develop some blues, but self-confidence will increase as the days go by.

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See page 176 for balance of references 17-28.

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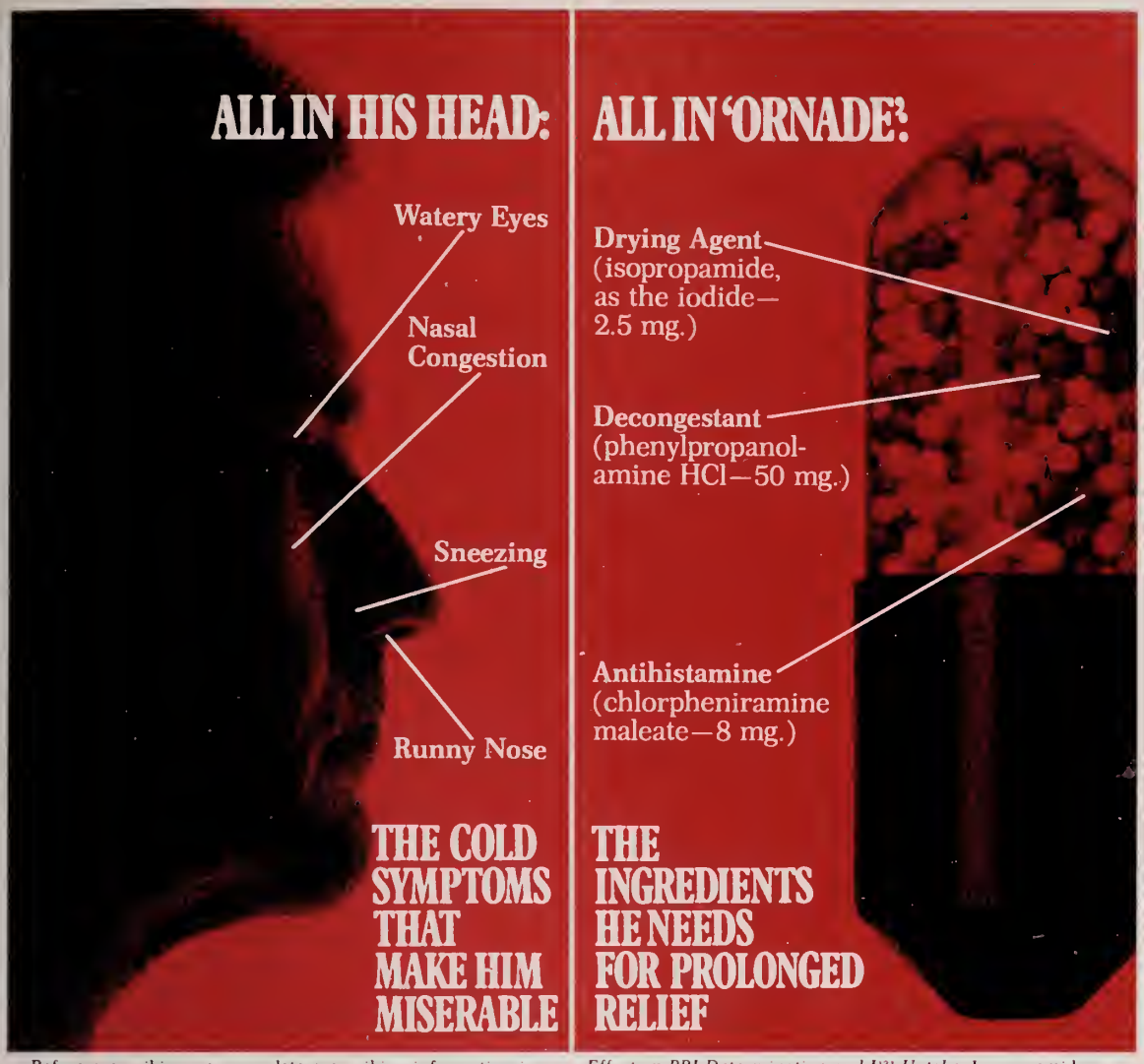
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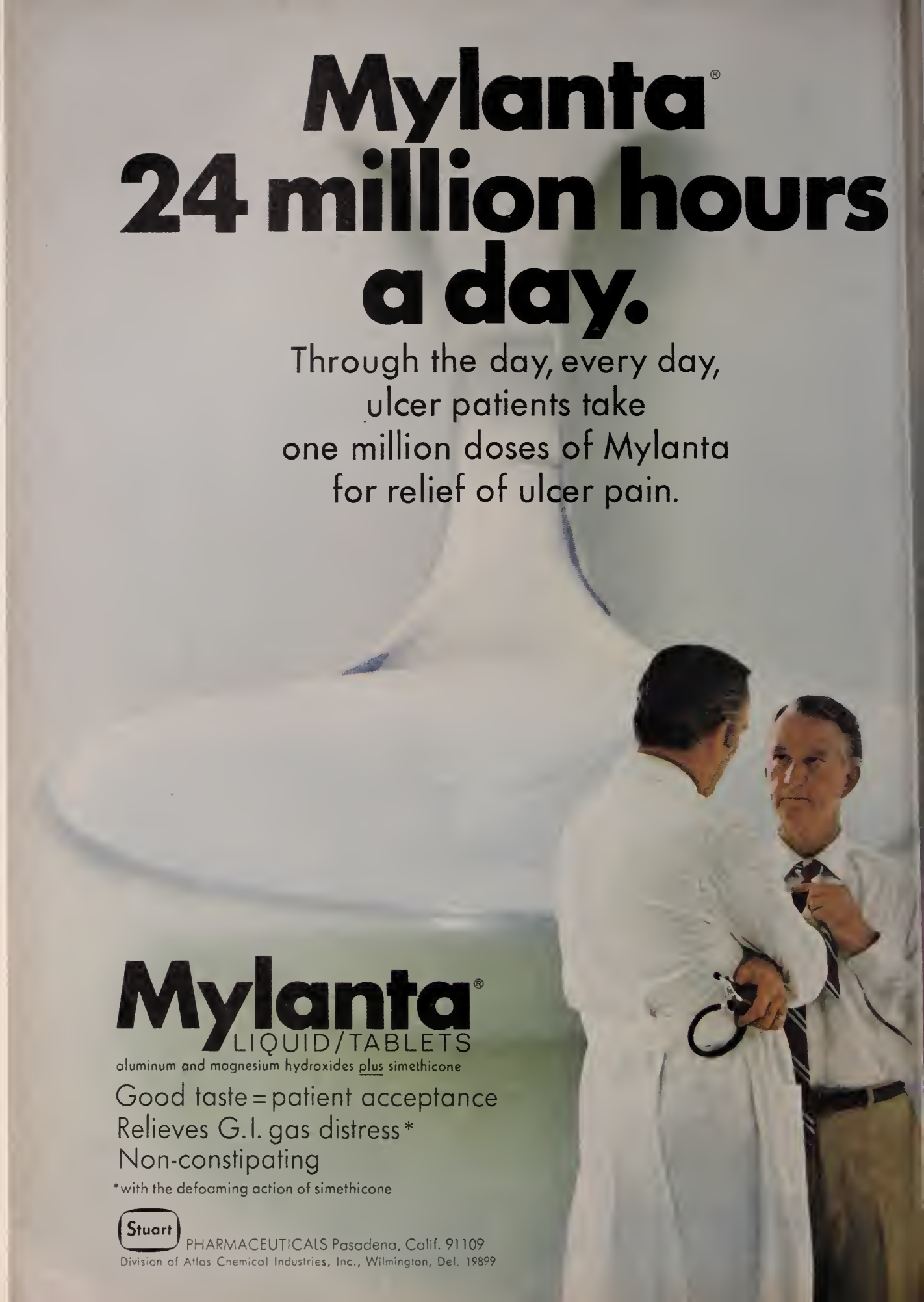
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The Story of The Childrens Hospital

ROBERT ROSENTHAL, M.D.*

INSTITUTIONS FOR THE CARE of children first took the form of foundling homes or hospitals during the early Middle Ages, even though always throughout the ages there have been parents who were either unable to care for their offspring or who were ashamed to acknowledge their paternity for fear of social criticism, and, in some cases, of ostracism from society. Foundling institutions, born out of compassion and pity for helpless waifs, appeared throughout Europe and in the Middle East. Unfortunately, these children's homes acquired poor reputations, because of the incredibly high mortality rate among their inmates. It is said, perhaps in a grimly jocular vein, although with enough truth, that in one year in a single home the death rate was 107 percent! The explanation of this astonishing figure is that not only did all the children admitted in one year die, but also seven percent of the children admitted the previous year. No better evidence could be put forth to underscore both the lack of proper general care and the lack of even elementary medical treatment in these early institutions.

Dispensaries

We might ascribe the beginning of the movement leading to the development of children's hospitals to dispensaries for children. The first of these was George Armstrong's Dispensary for the Poor Infants, opened in London in 1796. His service, because of lack of funds, continued for only a few years, but the idea grew. Eight years later, the first such dispensary was organized in Vienna, Austria. The history of children's hospitals, it will be seen, is not as long as sometimes thought. Yet, throughout the eighteenth century, there were no children's hospitals as such. Children, needing hospitalization, were placed in regular hospitals which were frequently so overcrowded that the children were placed either in beds with adults or in beds with several other children.

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Children's Hospitals

Overcrowding was such a problem in Paris at the *Hotel Dieu* that it prompted some forward-looking individuals to organize the first hospital solely for children. This was the *Hõpital des Enfants Malades,* established in 1802 by reorganizing an orphanage for girls, the *Maison de l'enfant Jésus,* into a three-hundred-bed hospital to care for children between the ages of one and one-half years and 15 years. Children, transferred from other institutions, rapidly filled the new hospital. A serious attempt was made to reject youngsters suffering from obviously contagious diseases.[1] For the first time in the history of pediatrics the diseases of children could properly be studied and the results of treatment observed.

Not until 1834 was the second such institution founded, the Nicolai Hospital in St. Petersburg. In 1841, another was opened in Ludwigsburg, Germany. Within the next two decades, two more institutions were established in Russia, and one in Hungary and another in Sweden. Not until 1855 did the movement for special hospitals for children reach the United States. In that year Philadelphia opened the first hospital for children of the poor in this Country, but it provided only 12 beds. During the next decade, hospitals in Chicago, New York, and Boston were founded. Seven more such institutions were opened in various cities during the 1870's and four more during the 1880's. Almost every large city enjoyed the benefits of a hospital for children during the first decade of the twentieth century, but there was none in the northern zone from Chicago to the Pacific coast.[2]

The Founding of The Children's Hospital in St. Paul[3]

St. Paul, lay in the neglected northern zone, and the crying need of a children's hospital in Minnesota was noted by Dr. Walter Reeve Ramsey. Ramsey, of Scotch ancestry and born in Canada, studied medicine at the University of

Maryland and was graduated in 1896 from the University of Minnesota medical school. The study of the diseases of children and of their treatment intrigued him early in his professional career, and, although he started in general practice, his interest in pediatrics steadily increased. He soon was placed in charge of the pediatric department of the City and County Hospital in St. Paul. He took postgraduate training in Boston and New York and soon began to teach pediatrics at the University of Minnesota. After further intensive postgraduate studies in Vienna and Berlin, he returned in 1902 and became the first physician to limit his practice to pediatrics in this area. He organized the first Baby Welfare Clinics in 1911 and devoted time to writing books pertaining to infant care, infant feeding, and the nursing care of children. Although his work was interrupted by service abroad during World War I, Ramsey continued to study his specialty. He was especially interested in childhood tuberculosis and visited various tuberculosis clinics, including Rollier's in Switzerland.[4]

With his war service behind him, Ramsey purchased five lots on Pleasant Avenue near St. Luke's Hospital, an ideal site for his proposed hospital. The lots sloped upward and faced south, so that the structure he conceived would be both well supplied with sunlight and equally well protected from north winds. Funds were raised with difficulty and the institution was incorporated by the spring of 1923. However, Ramsey's first hospital was opened, not on the fine spot he had purchased, but in an old, frame building adjacent to and owned by St. Luke's Hospital. Over the entrance he proudly hung a sign "Children's Hospital, Inc." This sixteen-bed institution was governed by a Board of Trustees and was used for four years. St. Luke's Hospital provided all laboratory, xray, and surgical facilities.

Meanwhile, Ramsey saw the cornerstone laid on August 24, 1927 for a children's hospital on the original site he had purchased. On that occasion, Ramsey's old friend, Dr. Issac Abt, of Chicago, delivered the dedicatory address. On July 23, 1928, the three-story building was formally opened to patients. Ramsey held the unpaid position of medical director and the active staff consisted of 15 physicians.

At the first staff meeting held in the basement meeting hall, the initial officers were elected. The members present unanimously elected Dr. James Trent Christison, chief of staff, because he was the oldest member and because he was the first of the group to teach pediatrics at the University of Minnesota. Indeed, Christison taugh pediatrics before Ramsey did, but he did not restrict his practice as early as had Ramsey. Ramsey was not elected chief because of his position as medical director. Christison, somewhat reluctant to accept the chief-of-staff post, said that "at my age" (he was only 63) "I prefer to sit by the fire and read a good book instead of going to a staff meeting." However, he fulfilled the post creditably. In 1944, when almost 79, he suffered a severe hip injury and died shortly thereafter. Christison, like Ramsey, was of Scotch descent, spent his childhood in Canada and was graduated from the medical school of the University of Minnesota.

The Early Years

In 1928, when the Children's Hospital formally opened, seven patients were transferred from the old, frame house at the corner of Smith and Walnut streets. Historically, practically all children's hospitals began primarily as charity hospitals, but the St. Paul institution initiated the policy of permitting patients to pay what they could afford. The minimum rate was $2.50 a day, and 80 percent of the early patients paid this fee. Patients were never designated as charity cases, but as free, part-pay, or full-pay individuals. During the first year, one percent of the patients fell into the free category, three percent



Fig. 1—The orginal hospital, at the corner of Smith and Walnut, St. Paul, Minnesota.

into the part-pay category, and ninety-six percent into the full-pay classification. Ramsey conceived of the hospital serving the "Great Northwest" and during the first nine months of the institution's life, 79 percent of the patients were from St. Paul, 14 percent from Minnesota areas beyond St. Paul, and seven percent from states other than Minnesota. Expenses exceeded income and by the end of the first year of operation there was a deficit of almost $30,000.

The active staff was comprised of all the pediatricians in St. Paul, who in conjunction with other physicians forming the associate and consulting staff, provided excellent service. Those on the consulting staff were required to give free service to free-bed patients. An educational program, in keeping with Ramsey's ideas, was begun during the first year and a school for nurses was begun. A graduate house physician was on duty part of the time, and arrangements were made with the University of Minnesota to accept a "fellow" for postgraduate research work.

An intern program, even though the depression of 1929 made progress difficult, was instituted, but not even the growing economic dislocation prevented an increase of patients. In 1928, 681 patients were admitted, in 1929, 1,316 and in 1930, 1,435. In addition 230 outpatients received attention in 1930. A bi-plane fluoroscope, to aid in the removal of lung foreign bodies and in setting fractures was acquired in 1931, the first of its kind in the Northwest. In that year, the Hospital published a textbook of pediatric nursing based on practices used in the hospital.[5]

Unfortunately, the continuing depression resulted in fewer and fewer paying patients, and every year witnessed a deficit. Admissions dropped to 999 in 1932, which was 436 less than during the previous year. Meanwhile, in a period of 12 months, the average daily cost per patient increased from $4.56 to $5.82, but the average daily income had risen only to $3.45. Some services were curtailed, floors were closed, salaries cut, and fees reduced for laboratory technicians and anesthetists. During 1932-1933, admissions dropped by another 270 patients and the daily income per patient was only $3.00. The monthly operating budget was cut $3,500, and the first and third floors were closed. The salaries of employees receiving full maintenance were reduced by 40 percent and wages of employees living outside of the hospital were slashed from 20 to 30 percent. The nursing school was closed. Despite these economies, the operating deficit was $11,200.

The Hospital Survives the Depression

Gradually, as the national and local economy improved, conditions slowly grew better for the hospital. A fear that the institution might be forced to close gradually gave way to confidence. During 1934 sixty-three more patients were admitted, and by the close of the year the financial situation was improving. This was due in part to the creation of the Junior League of The Children's Hospital Assocation, a group organized to raise funds for free beds.

The School of Nursing was re-opened in 1935; 1,210 patients were admitted, 418 more than in the previous year; 944 more laboratory tests were made; and 247 more major operations were performed. The next year an intern affiliation was instituted with Miller Hospital, and this service was much appreciated by the attending staff. During 1936-37, the third floor was re-opened, and there was an increase in admissions, laboratory work, and surgery. In the years 1937-38, a period when the Minnesota Hospital Service or Blue Cross became a factor in hospital income, 49 percent of the income for hospital services came from sources other than pay patients. The accounting system was changed to the calendar year. During this period The Children's Hospital Association contributed $16,000.

During 1939-40 all hospitals were busy, and many physicians brought patients for the first time to Children's Hospital. Infantile paralysis victims were cared for at Children's Hospital when funds were available, while awaiting care at Gillette Hospital.

World War II Years

The Hospital's annual report for 1942 stated it was "the busiest year in its history and certainly the most turbulent." For one thing, five members of the medical and two of the nursing staffs left to serve in the armed forces. This loss, coupled with the deaths of Dr. Harry P. Ritchie and Dr. George Hagaman, placed additional burdens upon those who remained. Ritchie was noted far beyond the boundaries of Minnesota for his plastic surgery. Hagaman was an excellent pediatrician endowed with great practical knowl-

edge. The year also witnessed the inauguration of the Federal Heart Clinic, under the auspices of the State Department of Public Welfare and directed by Dr. Paul Dwan, University of Minnesota. Patients in this clinic remained in the hospital for long periods of time. Other changes and improvements included the moving of the laboratory to better quarters, the installation of a portable electrocardiograph and the purchase of a portable x-ray unit and a battery-powered light for use in the operating room in the event of a general power failure.

Dr. Yoshio Sako was hired in 1943 as an assistant laboratory technician. He served also as junior intern and in this capacity exhibited such unusually good training that he proved an invaluable addition, especially since it was difficult for Children's Hospital to secure continuous intern coverage from the other St. Paul Hospitals. A better teaching program utilizing free-bed patients was developed, and the number of patients increased considerably. The acquistion of a Leitz colorimeter enabled Children's Hospital to make laboratory tests which previously were done at Miller Hospital.

The Hospital Grows

During 1945, a period of change and expansion, the Children's Hospital became affiliated with the University of Minnesota with Ramsey securing $1,200 annually for such a relationship. The staff numbered 14 pediatricians, nine surgeons, four orthopedists, 13 eye-ear-nose and throat specialists and one pathologist. Mr. Harold Bend, a year earlier, had equipped the large operating room as a memorial to his wife. A fourth floor, somewhat smaller than the original ones, was added because of increasing demand for beds, and the daily average census almost immediately increased by 14%. Supplies, now that the war was over, became both more plentiful and more costly. In the five years between 1940 and 1945, the price for hospital supplies rose 40 percent with yet another increase of 20 percent the following year. Two interns instead of one were obtained from Miller Hospital and the University of Minnesota furnished both a rotating resident and intern each quarter. The yearly admissions passed the 2,000 mark.

Miss Eleanor Sackett, assistant superintendent, became director in August, 1947, a post she held until 1970. During those years of decisive developments, her gift of organization and her equally important quality of tact promoted harmony among the staff, residents, interns, personnel, and the board. Yet she faced serious problems. It was necessary, for example, in 1948 to close the second floor because of a shortage of trained nurses. She played a prominent role in plans for expansion. She interested herself in a newly organized volunteer play-lady program. With the annual payroll increasing to 65.5 % of the total hospital expenses, it became necessary to steadily increase the cost of rooms.

The year 1952 marked the tenth anniversary of the beginning of the Federal Heart Program. The hospital cared for about 50 patients annually in the program. The average length of stay of patients in this program had been reduced from 87 to 25 days. During 1953, as the result of a survey by hospital experts, an expansion program was begun. A campaign to raise $2,250,000 was begun. The surgical suite, financed by The Children's Hospital Association, was remodeled. An anesthesiology department, headed by Dr. Ellis N. Cohen, was formed and resulted in a major improvement in the hospital's surgical



Fig. 2—Eleanor M. Sackett, administrator from 1947-1970.

performance. Because of lack of state funds, the Federal Rheumatic Clinic was discontinued in 1955.

The Enlarged Hospital

On July 22, 1957, ground-breaking ceremonies for the first phase of the new addition took place, but this was not the only significant event in the history of the institution. Ramsey had retired as medical director. Interns now rotated monthly, coming from the University of Minnesota and local hospitals. St. Luke's Hospital furnished a two-year resident, and, shortly thereafter, another came from Midway Hospital. By September, 1959, the new addition had been completed and all patients transferred to it. The East Wing was remodeled, and the Peter Pan Coffee and Gift Shop opened. The new addition was named "Lang Wing" to honor Mrs. William Lang, who, through the years, devoted so generously of her energies to the institution. The completion of the building project was celebrated on April 30 and May 1, 1960 with an open house. The old wing, now remodeled, was called the "Ramsey Wing." It included a communicable disease unit, so that, for the first time, the by-laws of the hospital could be altered to permit *any* patient, without exception, to be admitted regardless of his medical condition.

Although the new wing and changes in the older parts of the building greatly increased the total amount of space, they did not add greatly to the hospital's capacity for care of more patients. Indeed, room was provided for only 25-30 percent more patients. New space was devoted to the x-ray department, the laboratory, the out-patient department, the library, the dining room and administrative offices. A general feeling prevailed that the Hospital was at the "threshold of planning new services for health care for children in our community."

This proved to be true, for the institution during the 1960's did forge ahead. An Intern Education Coordination Program, under the supervision of Dr. Martha Burke-Strickland, was developed with the result that interns were given better learning experiences and patients received closer supervision. The program permitted the admission of more critically-ill children, especially newborns with respiratory difficulties. As a result of Dr. Strickland's excellent teaching instruction and equally fine nursing care the house staff was able to render superior care to critical infants. In 1964, two years after the program started, Dr. Strickland's title was changed from Coordinator of Intern Education to that of Director of Medical Education. The program now drew residents from the Department of Pediatrics of the University of Minnesota and in 1965, two University residents rotated through the Hospital every three months. Plans for Children's Hospital own residency program were made this year and grand rounds and all-day seminars were also instituted.

Peaceful progress was interrupted in 1964 when a dispute developed between the hospital administration and the housekeeping personnel. The latter, in violation of state law, went on strike. The loss of help crippled the institution in several ways and made the task of feeding patients especially difficult. Following a court injuction, most of the workers returned to their jobs. The strike was resolved by arbitration. Not



Fig. 3—The Lang Wing, opened in 1959.



Fig. 4—Eleanor M. Sackett and Dr. Ramsey at the ground breaking ceremony in 1957.

even the strike, however, prevented the hospital from enjoying a successful financial season. Admissions rose to over 4,900.

The increased patient load plus an admirable educational program prompted the institution to gather all its educational functions under the jurisdiction of a single Education and Research Committee, which was to be responsible for the scientific programs for staff meetings, special lectures, and seminars. The hospitals own residency program was approved, and the appointment of a surgical resident, affiliated with Miller Hospital, was effected. With the expansion of its intensive program in medical education, Children's Hospital was well on its way towards becoming a center for pediatric research, a function which Ramsey had envisioned from the beginning. More and more children were being referred to the Hospital for difficut diagnostic problems and intensive care. The residency program was further strengthened, and the first Children's Hospital resident began his training July 1, 1966. At the same time, a new medical student clerkship training program and a program in intensive care for nurses were initiated. An intensive care unit for newborns, a unique service in midwestern states, began operating in 1967. Dr. Krishna M. Saxena joined the staff as Associate Director af Medical Education, and he encouraged members of the pediatrics department of the University of Minnesota to come to Children's Hospital for conferences and rounds. Thus, the relationship between the hospital and the University became closer.

The Children's Hospital Clinic was officially opened on January 3, 1968, replacing the pediatric department of the St. Paul Medical Center, which had closed at the end of 1967. The clinic's transition was accomplished without any lapse of service and the new clinic continued to play a vital role in the training of house staff. During the first year of the clinic there were 5,146 visits by the 250 families covered by the comprehensive health program. Dr. Strickland resigned during the year, after serving half a decade, and Dr. Saxena succeeded her as Director of Medical Education. Admissions, during 1968, numbered over 4,000 and days of patient care totaled 28,900.

The year 1969 offered an excellent vantage point for retrospect and summation of progress made during the decade. The completion of the



Fig. 5—Ward A. Stoddard, Administrator of The Childrens Hospital.

Lang Wing inspired a new era of specialized care; the expanded facilities of the x-ray department and laboratory provided new diagnostic techniques; the intensive care unit for newborn infants rendered a unique service in the area; increased library holdings, the appointment of a full-time librarian and the revamped dietary department, were models of planning and efficiency; the closer relationship of the hospital with the pediatric department of the University of Minnesota brought mutual benefits; and the approval for the hospital's own residency program was a great forward stride.

A new addition to the hospital, begun in July, 1969, was completed early in 1970. Although the additional space which the addition provided will not solve the institution's future needs, it does permit the hospital to presently function more efficiently and effectively. That the institution is growing is evidenced by the following 1969 statistics: over 4,000 inpatients and almost 7,300 outpatients; 5,600 clinic visits; 610 major operations and 389 transfusions. On January 4, 1971, Ward A. Stoddard became administrator.

The Childrens Hospital may well be proud of its growth and accomplishments during the forty-two years since it first opened its doors. Of the original pediatric staff, three continue to be active, one is connected with the Faribault School for Retarded Children, two have moved from St. Paul, one has retired, and the others have passed away. Dr. Ramsey, who, at ninety-nine years, remains in good health, is mentally keen, and watches with utmost interest the fulfillment of his dream of long ago.

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Doctor Francisco Grande Awarded First Spanish Prize

Dr. Francisco Grande, Director of the Jay Phillips Research Laboratory at Mount Sinai and Professor of Physiology at the University of Minnesota Medical School, has been awarded the Rodriguez Pascual Prize for medical research.

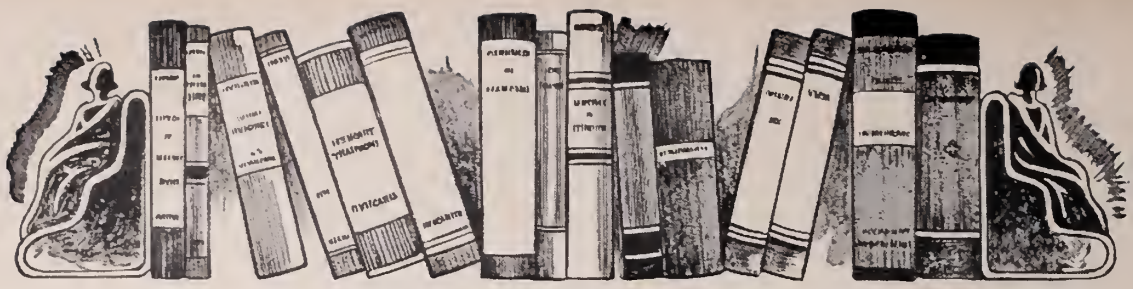
Awarded for the first time, this prize has been recently instituted by the Spanish philanthropist, Eugenio R. Pas, Marquis de Pelao. It is given to Dr. Grande "in recognition of his contributions to medical knowledge throughout a lifetime devoted to research in the basic sciences of medicine."

The prize was given to Dr. Grande in a ceremony taking place in the College of San Carlos, a building of the Madrid University Medical School, January 24, 1972. At that time Dr. Grande lectured on "Hormonal Control of Fatty Acid Mobilization," describing his work currently involved at the Jay Phillips Research Laboratory at Mount Sinai.

Born in Colunga, Spain, Dr. Grande graduated summa cum laude from the Madrid University Medical School with his doctorate of medicine. Various working positions in physiological laboratories in Spain, German, Denmark and Wales brought Dr. Grande in contact with the world's outstanding researchers in physiology.

The amount of the prize is two million pesetas, about $30,000.

For the cause that lacks assistance,
The wrong that needs resistance,
For the future in the distance,
And the good that I can do.—George Linnaeus Banks



Book Reviews

HANDBOOK OF LEGAL MEDICINE by Helen R. Morritz, M.D.; C. V. Mosby Co., 1970; Price: $8.75; Pages: 238.

For the physician who ordinarily is not well versed in the legalities of medicine, his conduct in court, his privileges and responsibilities under the circumstances of expert testimony, this Handbook is an excellent source of reference.

The first part deals with scientific, medical, legal investigation, and the second part deals with the physician, the patient and the law. In the second part the medical legal liability of the physician in relation to his patient is adequately dealt with.

There are about 16 human interest sketches depicting most of the commonly encountered medical-legal problems of which physicians are aware: criticism of another physician, the importance of reliable laboratory diagnostic aid, avoiding a delay in diagnosis, guaranteeing a cure, the need for xrays in bone injury, and other problems that are commonly discussed in the staff room, so that the answers are usually known.

The book is nicely edited and well bound. Page headings might have been of additional value for thumbing purposes.

Carl O. Rice, M.D.
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INSTRUCTIONAL COURSE IN LECTURES; C. V. Mosby Co.; Price: $19.50.

The series of manuscripts in this volume are by a group of authors, all of whom are well qualified to deal with the problem that they have chosen. Each of the 13 topics is significant to the practicing physician who deals with injuries or orthopedic diseases. They constitute, on the whole, the most commonly encountered problems and should be constantly in the mind of the clinician.

Adequate but not exhaustive bibliographic references are included. The volume is well bound and beautifully illustrated.

Carl O. Rice, M.D.
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BIG FLEAS HAVE LITTLE FLEAS by Robert Hegner; Dover Publications, Inc., New York; $2.00.

This is a fascinating book with cartoon illustrations loaded with information and facts about the protozoa. It was almost shocking to read that every organ and every tissue in our body may be so well parasitized with protozoa that were our body "to disappear entirely, leaving behind only the parasites, a perfect outline of the human form would remain, and even the features would be so clearly discernible that individuals could be recognized."

I recommend it for an hour of intellectual and fascinating reading.

Carl O. Rice, M.D.
Minneapolis, Minnesota

RENAL DISEASE IN CHILDHOOD by John A. James, M.B., M.R.C.P., D.C.H.; C. V. Mosby Company, St. Louis; Publication date: 1968; Price: $18.50.

An excellent book, concise and practical, with special emphasis on diagnosis and treatment of renal diseases in children. As such it will be particularly useful to physicians in training and practice who care for renal diseases in children as part of a larger group of patient problems. Discussions of etiology and pathology are brief and adequate. Choice and selected references are appended to each chapter for physicians who become interested and desire further information.

The final chapter on dialysis and homotransplantation offers steps from the practical into the highly technical, controversial, and rapidly changing areas of research and therapy. This chapter seems a forced after-thought in a practical book since both of these subjects might well have been handled in the discussion at the end of the chapter on renal failure. However, this is a minor defect, for the first fourteen chapters of the book are excellent and justify wide acceptance of this book by its intended audience.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

SYNOPSIS OF DERMATOLOGY; Wm. D. Stewart, M.D.; Julius L. Danto, MD; and Stuart Maddin, M.D.; The C. V. Mosley Company; Price: $13.85.

This second edition of Synopsis of Dermatology is an excellent book for both students and practitioners. The text is divided into four sections. The first deals with the development, structure, and function of the skin. Second, the office practice of dermatology is discussed. Regional diagnosis is next covered; while the final section describes individual diseases.

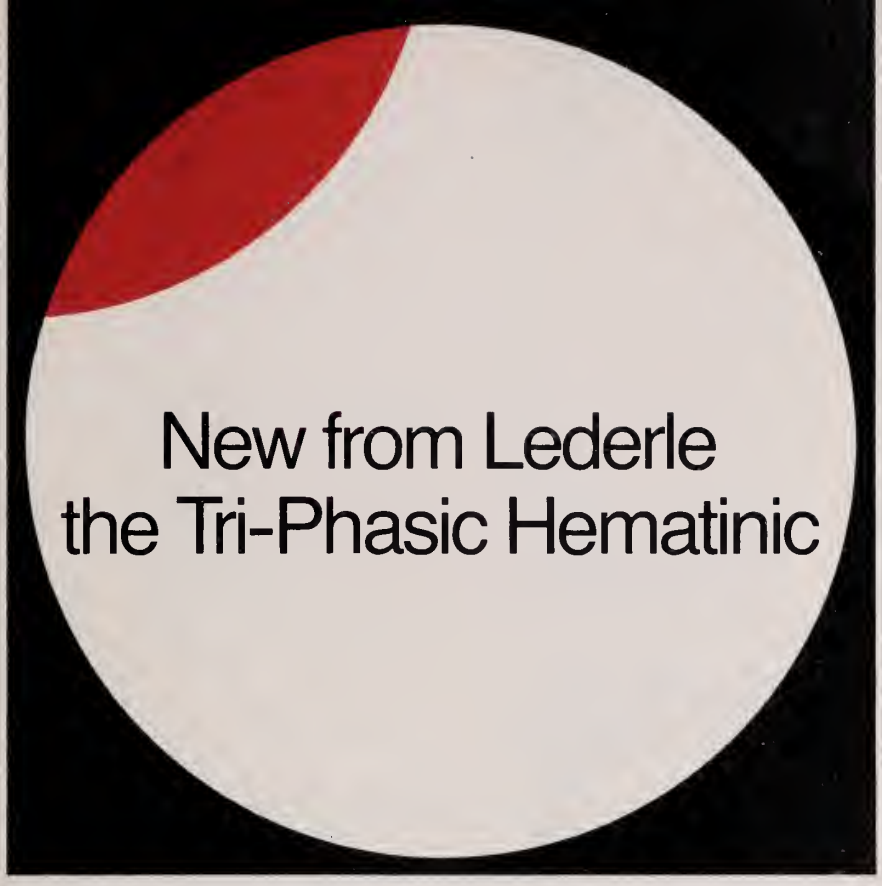
Discussions of the various dermatologic conditions are by necessity short in a book of this length (pp 445). However, the descriptions are adequate and well written. In addition, many of the newer concepts in both diagnosis and treatment of dermatologic disease are covered. For each disease, the authors, include a clinical description, differential diagnosis, and treatment. It should be noted that this book is well illustrated with many color plates, most of which are of excellent quality. This volume should be of value for those interested in clinical dermatology.

Willard Peterson, M.D.
Minneapolis, Minnesota

CURRENT DERMATOLOGIC MANAGEMENT by Stuart Maddin, M.D.; C. V. Mosby Co., St. Louis, Mo., 1970; Price: $38.75; Pages: 330.

This is an excellent book, not only for the dermatologist, who is surely aware of all of these diseases and recognizes them, but for any physician who is in practice and is interested in identifying skin diseases that may have to be referred.

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Minneapolis, Minnesota



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Diet and Diabetes

A New Approach to Planning Meals

GARIFALLIA MILLER, R.D.*

IN LOOKING CAREFULLY at today's management of diabetes, three facts emerge:

(1) That up to the present time no hypoglycemic agent has been developed that can synchronize its activity with blood sugar levels. Consequently, diet still remains an important factor in the treatment of diabetes. Doctors may disagree as to the goals the treatment should seek to achieve. Nevertheless, they all recognize that freedom from frequent annoying complications depends on some kind of regularity of feeding.

(2) The second fact is that except for the hospitalized diabetic, treatment and control is the individual diabetic's responsibility even from an early age. Diabetics, therefore, must know how to plan their meals themeselves.

(3) The emotional state of the individual affects his control. Most diabetics do well and are resigned to the necessities of injecting insulin and testing their urine. However a great many of them have difficulties adhering to any kind of a meal pattern. The teenagers especially are resistant to accepting any regimentation even though they may be aware of future consequences. Diets as a rule are too regimented, extremely monotonous and inconvenient. In most cases they demand too much from the patient and result in temptations, stresses, worries, periods of depression and guilt feelings.

The new method for planning meals, the *Guide To Meal Planning* was developed in an attempt to eliminate some of these frustrations. Our objectives were to make meal planning:

(1) Simple enough so that it becomes as automatic as getting dressed. Since it is the individual diabetic's responsibility to plan his meals, we felt that the simpler the method of determining the quantities of food and the ratio of protein, carbohydrate and fat in a meal, the easier it would be to remember and to follow.

(2) Flexible enough so that it would be easily adjustable to all situations. Years ago, temptations to eat forbidden foods were very few; however, nowadays our social life and advertising media make it quite difficult to avoid temptations. For children this is even more difficult. The diabetic should be taught how to incorporate some regular desserts in his diet, not only the so-called dietetic ones. We believe that a piece of regular cake, poorly substituted, is not as dangerous to the diabetic's control as the frustration of not eating it, or the sense of guilt after eating it in spite of its exclusion from the diet. It is very significant that up until we started showing how to incorporate some regular desserts in the diet patterns, diabetics would never admit they used them. Now it is a different story entirely.

The new method, the *Guide To Meal Planning,* is a simplification of the *Exchange Lists* method.

Exchange Method

In the last twenty years diabetics were taught to plan their meals with the *Exchange Lists* method. We found that diabetics, regardless of age, intelligence, or educational background had many difficulties with the exchange method. The word *exchange,* for instance, is very confusing. There are too many groups and too many measurements to represent one unit of food or one serving. This requires a great deal of memorizing, one more cause of resentment, and sooner or later the method is forgotten.

The "Guide To Meal Planning"

The first step for the simplification of the *Exchange Lists* method was to find another word to represent a unit of food that would be familiar and, therefore, easily accepted and remembered. The word *serving* was chosen. Secondly, we named groups of foods on the basis of composition. For instance, the meat group was called *protein foods,* the bread group was called *starchy foods.* Thirdly, we eliminated many measurements. A diabetic is now taught only three

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measurements, each to represent one serving or one unit of food. Fourth, except for three vegetables included in the starchy group, foods were listed in groups in the way people know them: proteins, milk, starches, fruits, fats, vegetables.

Description of the New Method

Based on their nutritive value, foods are listed in six groups.

Group 1—Protein Foods

In this group we have listed all foods high in protein, and it included:

(1) All meats. (2) All fish and seafoods, (3) Eggs and (4) Cheese.

We use the word *protein* to name this group because the word is well-known even among children, and because it is a word denoting composition and value of food rather than naming one particular food. For a unit of food, or one serving of protein food as it is called in this method, we use a slice of meat or fish, 2 x 3 x ¼ inch. This measurement is also identified on the palm of the individual's hand by tracing a rectangular figure approximately two by three inches.

Group 2—Starchy Foods

All foods high in complex carbohydrates are listed in this group and include:

(1) All flour products: (a) bread, (b) cereals and (c) macaroni, noodles, and so forth. (2) rice and rice products. (3) Three vegetables: (a) potatoes, (b) corn and (c) dry vegetables, legumes. (Carbohydrate content of these vegetables is the same as in all other foods listed in this group.) We named the group *starchy foods* because the word denotes composition. For a unit of food, or one serving of starchy food, we use one half cup.

Group 3—Fruits

All fruits are listed in this group. One serving of fruit is one half cup.

Group 4—Milk

Milk is listed separately. One half cup is used to identify one serving of milk. Greater amounts of milk allowed are identified as two, three or four servings. Depending on caloric allowances, individual preferences and modifications of one's diet, the type of milk an individual should have is marked as skim, 2% or 3½% butter fat.

Group 5—Fat

Butter, margarine, oils and salad dressings are listed in this group. For one serving of fat we use one teaspoon.

Group 6—Vegetables

All vegetables with the exception of the three listed with the starchy foods are included in this group. Listing vegetables into *A and B groups* in the *Exchange* method proved to be somewhat inaccurate. On the other hand, the higher carbohydrate content of a few *B vegetables* when these vegetables are used as *Free Foods* does not alter total average intake. Consequently, we felt there was no need to list the vegetables into two groups. All vegetables are listed in one group, and patients are instructed to use them in any amount—*Free Foods.*

The diabetic learns from this method:

(1) What is included in the group of protein foods.

(2) What is listed in the group of starchy foods.

(3) The three measurements: For proteins, a 2 x 3 x ¼ inch piece, one teaspoon for a fat serving, and one half cup for all other foods. This is all. The average protein, fat and carbohydrate content of a serving of food listed in each group is given in Table 2. The dietitian calculates the diet. The number of servings of proteins, starchy foods, etc. for each meal and snack are written in the space provided on the "Guide To Meal Planning" folder which we provide.

Besides this folder, a small billfold size card is given to the diabetic with this information on it (Table 1). In planning or choosing his meals,

TABLE 1
Billfold Size Card with Food Allowances for Each Meal
Daily Food Allowance

Breakfast:		**Midmorning Snack:**
Protein Food	1	
Starchy Food	2	
Fat	2	
Fruit	1	
Milk	1	2
Lunch:		**Midafternoon Snack:**
Protein Food	1	
Starchy Food	2	1
Fat	2	
Vegetable Any amount		
Fruit	1	
Milk	2	1
Supper:		**Evening Snack:**
Protein Food	2	1
Starchy Food	2	1
Fat	2	1
Vegetable Any amount		
Fruit	1	
Milk	2	1

the diabetic knows or refers to this card for the number of protein or starchy servings, etc., he is allowed at each meal and snack. This way he can easily detect shortages or excesses and make adjustments before serious consequences appear. Also, he can easily make reasonable changes in the basic meal plan to fit special daily demands.

Rationale

Our effort to make meal planning simple was definitely not at the expense of being within the range of safety for "good control." No method has been devised yet that could be used in planning accurately the food intake. For instance: A closer look at the "Exchange Lists" would reveal many discrepancies.

Here are two examples:

	Content		
	Cho	*Pro.*	*Fat*
½ cup noodles = 1 bread exchange	18.6 gms.	3.2 gms.	1.2 gms.
½ cup corn	16.4 gms.	2.1 gms.	0.6 gms.
Yet less corn (⅓ cup) is allowed for	one bread exchange		
½ cup wax beans	5.2 gms.	1.4 gms.	0.3 gms.
½ cup carrots	5.0 gms.	0.6 gms.	0.2 gms.

TABLE 3

	Actual Average Values of Foods in a Group				Food Values given to Groups		
	No. of Items Used	Pro.	Fat	Cho	Pro.	Fat	Cho
Fats	7	0	3.1	0.2	0	4	0
Fruits	33	0.7	0.2	12.6	0	0	15
Fruit-Juice	9	0.4	0.1	16.2	0	0	15
Milk—Whole	....	4.2	4.2	5.8	4	4	6
Starchy-Foods	26	2.3	1.0	14.9	2	0	15
Proteins	29	8.0	4.1	0.2	8	4	0
Vegetables	25	1.3	0.1	4.8	FREE FOODS		

However beans, although similar in CHO content to carrots, are listed in the A group of vegetables. The question then arises, why is it necessary to have patients memorize the different measurements or what vegetables belong to A group or B group? But let us examine another point. Depending on the cut of meat or the type of animal, in 100 gms. of meat, there is a variation of 10 gms. in the protein content to use just two examples. In a half cup of orange juice there is a variation of 5 gms. or more in the carbohydrate content. Furthermore, food manufacturers often alter food composition to the extent that many well established food tables are obsolete. For instance, meat may be injected with a starch product to hold in meat juices during cooking, yet is meat known to be a source of carbohydrate?

With this in mind the following question might be in order. Could we possibly expect and is it at all realistic to have patients memorize or refer to long lists and dozen of measurements in planning their meals? Food tables are good reference material, but one should know their limitations. Whenever an accurate food intake is necessary, a synthetic diet can be prepared. For the rest of the patients, a few general groups of foods and the minimum number of measurements should be quite satisfactory.

Flexibility

The *Guide To Meal Planning* is a tool that can be used in several ways and for many purposes. It can be used for weight reduction diets or normal nutrition education. The practitioner can use all or part of it. Modifications of the type or quantities of fat, cholesterol or sodium, can be marked on the booklet. Also a basic outline of diets with different caloric levels to meet individual philosophies of CHO, fat and protein ratio could be written and used as a guide.

Clear and Full Liquid Modifications

For a full liquid diet, patients are instructed to substitute protein servings with milk servings and starchy servings with fruit juices or pop on a one to one basis. For a clear liquid diet, 1 serving of protein or milk is replaced by half a serving of fruit juice.

Two Year Evaluation

The *Guide To Meal Planning* has been in use for over two years. In our hospital we instruct both parents and children, and thus we are able to evaluate its acceptance by both groups.

In evaluating the method we have the following to report:

1. It is a method simple and easy to teach.
2. Patients and parents understand and remember the method well.
3. Adjustments to the basic meal pattern are made easily.
4. Urine tests showed the same or better results after the change to the New Method. We have no patients reporting either worse urine tests or dissatisfaction.
5. Parents who changed to this method, reported that relationships with their children improved considerably.

6. Last, parents and patients reported a feeling of confidence and security in knowing how to plan meals easily and quickly. For the new diabetic this is of paramount importance.

Summary

The difficulty patients had in understanding the "Exchange Lists" method, the discrepancies in the average values of available glucose of foods within a group, as well as a closer examination of the limitations of food tables led to the development of a new, simpler and more realistic method. *The Guide To Meal Planning,* a general guide with only the basic foods included, was developed.

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Nursing

The Nurse and Hospital Emergencies

LOIS ANITA YOUNG, R.N.*

A NURSE WALKS into Room 206 to check her patient. The child is cyanotic and has stopped breathing. Immediately she calls for help and initiates emergency measures. Meanwhile, other personnel assigned to this nursing unit notify the switchboard operator by dialing 414, the hospital emergency telephone number. The emergency cart is brought to the patient's room.

The switchboard operator, on receiving the call, immediately broadcasts "Intern, Second Floor." To assigned medical and nursing staff this means "Report immediately to the second floor nursing unit. There is an emergency."

This is the emergency procedure used at The Childrens Hospital, Inc., Saint Paul, Minnesota.

Emergency carts placed in the treatment room of our nursing units and outpatient department have been found to be most helpful in managing emergency problems. A chrome lake-side cart with easy movable rollers has been adapted to contain the supplies, medications and equipment needed in an emergency. The easy visability and accessability from all sides and the placement of some of the items on small trays are all special features to aid the staff.

The first shelf contains a small tray with the laryngoscope, laryngoscope blades #0-#4, resuscitubes and airways; the suction, oxygen and feeding tubes are in clearly labeled packages. The syringes and needles are in a box beside a sealed plastic drug box. Some of the drugs are placed in styrofoam; labels up for easy reading. Another small tray contains the supplies needed for I.V. therapy. I.V. solutions stocked are: 5% dextrose in 0.33% saline—5% dextrose in 0.45% saline—5% dextrose in water.

Attached to the first shelf is a drawer divided into 16 compartments, which contain different sized hard and soft endotracheal tubes, batteries, laryngoscope bulbs and tracheotomy needles. To aid the staff in finding the necessary endotracheal tubes quickly, the labels are placed at the top of each compartment.

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The second shelf contains supplies needed for intravenous and blood therapy. The spinal manometer is alongside the spinal tap equipment, which has four spinal needles taped to the top of the box. An adapter is attached to the rectal tube ready for use.

The third shelf contains a large and small cardiac board, the Hope and the Ambu resuscitator with infant, child and adult masks, and two clipboards. One clipboard has pre-prepared medication labels (Example: Soda bicarb—dilantin), and the other clipboard has a resuscitation record for recording emergency events.

Special Courses

Besides a better equipped emergency cart, an indepth course titled, "The Role of the Nurse in An Emergency" for R.N.'s and L.P.N.'s has been developed. Full-time and part-time nurses (except Intensive Care and surgery personnel) are regularly scheduled to attend classes conducted by the Inservice Education Staff.

Session 1

The course consisits of a review of methods for reporting emergencies and the emergency code. A taped doctor's lecture titled, "The Role of the Nurse in An Emergency" discusses the signs and symptoms of cardiopulmonary arrest and the responsibilities that nurses may assume to assist at the emergency scene. For example, the role of members of an emergency team are discussed, listing responsibilities as follows:

Nurse 1—Will, on entering the room, place the cardiac board beneath the patient, assist in ventilation and resuscitation, assist in connecting the electrocardiogram instrument.

Nurse 2—Prepares and labels 10cc epinephrine 1-10,-000, 25-30cc sodium bicarbonate and calcium gluconate or chloride 2-3cc. Normal saline is then prepared for intravenous therapy.

Nurse 3—Acts as a record keeper. She charts all pertinent information about the patient. A special resuscitation form was designed to aid in recording when the emergency is over. Nurse 3 will also be responsible for replenishing the emergency cart for future use.

The supervisor, who can assist at the scene of the emergency if needed, is the traffic director, checks baptismal status of patient, talks to the parents, notifies the private physician, if he is not present, and obtains additional supplies and equipment.

The nursing staff has initiated and assumes these re-

sponsibilities now, whenever an emergency occurs.

Session 2

The film "Pulse of Life" or "Prescription of Life" is shown. All nurses practice mouth-to-mouth resuscitation and external cardiac massage.

Session 3

The discussion and demonstration of the emergency cart supplies and equipment has proven to be most helpful to the nurses. This is the "how to," "what to do" and "when to do" session. Many helpful suggestions are made. For example:

(a.) Attaching the laryngoscope blade to the handle is easy and can be done quickly when inserted at a 90° angle, pressed by the thumb and a click is heard, or

(b.) If flashlight batteries are inserted button up, they will make the necessary contact and light up immediately, or

(c.) If you drop the cardiac needle—maybe the spinal needle can be used, or

(d.) How to use the Hope and Ambu resuscitators, or

(e.) How to set up intravenous solution quickly without air bubbles.

It's the "knowing how" and "what to do" that gives the nurse confidence to assist efficiently in an emergency.

Session 4

This session is a discussion of emergency drugs by the hospital pharmacist or inservice instructor.

Session 5

During this session, demonstrations of the cardiac monitor, I.P.P.B. respirator, and oxygen equipment are given by the inhalation therapist.

Session 6

"Listen and Learn."

We allow time for the nurses to discuss problems they have encountered during an emergency situation. They are encouraged to suggest improvements that might help the next time an emergency arises. During one month's classes, thirty-one recommendations for improvements were made. Thirty of these were instituted.

Session 7

Each nurse is given an opportunity to practice in a simulated emergency situation using the emergency cart and Resusci-Anne. An Inservice Education staff member acts as the doctor. The nurses take turns as Nurse 1, 2 and 3.

There are postchecks which aid in determining the effectiveness and success of the course. The nurses, working in teams of two, are required to:

(1.) Practice together two times, by a stated date;

(2.) Report for final evaluation by an Inservice Education staff member or assigned person.

Each assignment is to be completed by a predetermined date. (Appendix D.)

The use of audio-visual aids has helped to strengthen the program. The films "Pulse of Life" and "Prescription of Life" are obtained from the Minnesota Heart Association. The Resusci-Anne and Resusci-Baby manikins were donated to us by the Medical Staff and Board of Trustees. A tape recorder is used to tape all lectures. Our doctors donate many hours of lecture time to nursing education. We are also fortunate to have a demonstration emergency cart to use for all class sessions.

Conclusions

The nurse aides know the location of the emergency carts and have been taught mouth-to-mouth resuscitation. The ward secretaries also know the location and contents of the emergency carts.

We are now planning the use of an emergency resuscitation team in the future. When the emergency telephone number is dialed to notify the switchboard operator of a cardiopulmonary arrest, she will also be given the room number. She will broadcast, "Dr. Blue, Room Number —." Assigned staff, the resident, intern and medical student assigned to the nursing unit, three nurses and a supervisor will respond to the alert.

The concern, interest and assistance of our medical, nursing, and other hospital staff has improved the quality of our emergency program. We will continue to ask for suggestions and ideas from those people who are most involved in the care of patient emergencies.

Had old Hippocrates or Galen,
That to their books put med'cines all in,
But known this secret, they had never
(Of which they will be guilty ever)
Been murderers of so much paper,
Or wasted many a hurtless taper;
No Indian drug had e'er been famed,
Tabacco, sassafras not named;
Ne yet of guacum one small stick, sir,
Nor Raymond Lully's great elixir;
Ne had been known the Danish Gonswart,
*Or Paracelsus, with his long sword.**

---

*Ben Jonson: Volpone, 1607. "Song" (for a quacksalver).

Laboratory Letter

Osmolality

SOME YEARS AGO H. L. Gold wrote a little story about a man who got into trouble with the elves of a certain lake. As punishment the elves decreed that water would actively stay away from him. Since he was at the lake primarily to fish, but wanted also to bathe and drink, the results of the decree proved frustrating to the hero and amusing to the reader.

Now both disease and therapy can alter man's body water, particularly the concentration of elements in it. But unlike the situation of the hero in Gold's story, diagnosing and managing patients with disorders of hydration more often frustrates than amuses. This is true whether one is dealing with the life-threatening hypertonic dehydration of viral enteritis, or the factitious hyponatremia of hyperlipemic states.

Substances dissolved in water exert an osmotic effect. This osmotic effect causes water to move through cell membranes, swelling or shrinking individual cells, increasing or decreasing tissue edema, or even producing hyper- or hypovolemia.

Osmotic pressure can be measured in various ways and with various instruments. At one extreme it can be estimated, which is essentially all we do when we measure serum sodium, while at the other extreme it can be measured directly with a semipermeable membrane, a technique requiring so much sample as to be completely impractical. In practice, we take advantage of the fact that osmotic pressure, boiling point, freezing point, and vapor pressure are tied unalterably together. For example, the more salt one dissolves in water, the higher the osmotic pressure and the lower the freezing point become. Thus, in the clinical laboratory, we can determine the osmotic pressure of a sample of urine or serum by measuring its freezing point.

There are several practical advantages to measuring osmolality by this method. First, it is a quick test with the answer available within minutes after separation of the serum from the clot. Second, it is a non-destructive test and after determination of the freezing point, the sample can be thawed and used for some other determination. Third, it is a "micro" test and utilizes a sample volume of only 0.2 ml, an important consideration in ill infants. Fourth, it is a highly reproducible test. Over the years our pooled, control serum has demonstrated a standard deviation of $\pm$ 2.0 mOsm/Kg.

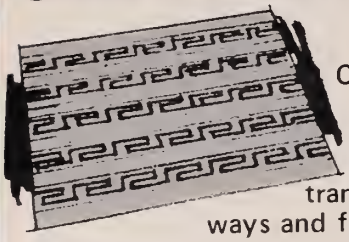
Osmotic pressure is reported in terms of osmolality (a mole of any substance dissolved in a kilogram of water has the same osmolality—or osmotic effect—as a mole of any other substance). Osmolality is most conveniently reported as milliosmoles per kilogram of water. Normally, serum osmolality is 285 $\pm$ 5 mOsm/Kg of serum water. Urine osmolality varies quite widely, depending on the state of concentration, but is usually in the range of 600 - 1400 mOsm/Kg. The newborn kidney, however, is not capable of concentrating much above 700 mOsm/Kg.

Osmolality is a most valuable screening test for dehydration. If the osmolality is normal, sodium and other solutes are usually normal. An osmolality above 300 mOsm/Kg is indicative of hypertonic dehydration. Serum osmolality is also a useful test for differentiating true hyponatremia from artifactual hyponatremia. The simultaneous determination of osmolality in urine and serum both before and after administration of pitressin is a useful confirmatory test of diabetes insipidus. As a measure of urinary water, osmolal clearance and free water clearance are indicators of antidiuretic hormone activity.

This is only a brief review of a test which can yield more information than its relative speed, and ease of performance might indicate.

Charles W. Jarvis, M.D.
St. Paul, Minnesota

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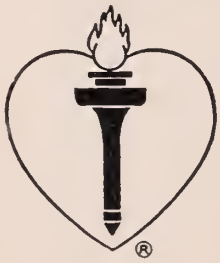
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INDICATIONS: Phenoxymethyl penicillin is indicated in the treatment of mild to moderately severe infections caused by penicillin G-sensitive microorganisms that are sensitive to the low serum levels common to this particular dosage form. Therapy should be guided by bacteriological studies (including sensitivity tests) and by clinical response. Culture and sensitivity testing are especially important in suspected staphylococcal infections because increased resistance has been reported. Phenoxymethyl penicillin is not active against penicillinase-producing bacteria.

Note: Severe pneumonia, empyema, bacteremia, pericarditis, meningitis, and arthritis should not be treated with phenoxymethyl penicillin during the acute stage.

Indicated surgical procedures should be performed.

Medical conditions in which oral penicillin therapy is indicated as prophylaxis: For the prevention of recurrence following rheumatic fever and/or chorea. To prevent bacterial endocarditis in patients with congenital and/or rheumatic heart lesions who are to undergo dental procedures or minor upper respiratory tract surgery or instrumentation.

Note: Oral penicillin should not be used as adjunctive prophylaxis for genitourinary instrumentation or surgery, lower intestinal tract surgery, sigmoidoscopy and childbirth.

CONTRAINDICATION: A previous hypersensitivity reaction to any penicillin.

WARNINGS: Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. While more frequent following parenteral therapy, anaphylaxis has occurred in patients on oral penicillins. These reactions are more apt to occur in individuals with a history of sensitivity to multiple allergens.

Some individuals with a history of penicillin hypersensitivity reactions have experienced severe hypersensitivity reactions from a cephalosporin. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, the drug should be discontinued and the patient treated with the usual agents, e.g., pressor amines, antihistamines and corticosteroids.

PRECAUTIONS: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

The oral route of administration should not be relied on in patients with severe illness, or with nausea, vomiting, gastric dilatation, cardiospasm, or intestinal hypermotility.

Occasional patients will not absorb therapeutic amounts of orally administered penicillin.

In streptococcal infections, therapy must be sufficient to eliminate the organism (10 days minimum); otherwise the sequelae of streptococcal disease may occur. Cultures should be taken following completion of treatment to determine whether streptococci have been eradicated.

Prolonged use of antibiotics may promote the overgrowth of nonsusceptible organisms, including fungi. Should superinfection occur, appropriate measures should be taken.

ADVERSE REACTIONS: While the incidence of reactions to oral penicillins is much less than with parenteral therapy, it should be remembered that all degrees of hypersensitivity, including fatal anaphylaxis, have been reported with oral penicillin.

The most common reactions to oral penicillin are nausea, vomiting, epigastric distress, diarrhea, and black hairy tongue. The hypersensitivity reactions reported are skin eruptions (maculopapular to exfoliative dermatitis), urticaria and other serum sickness reactions, laryngeal edema, and anaphylaxis. Fever and eosinophilia may frequently be the only reaction observed. Hemolytic anemia, leucopenia, thrombocytopenia, neuropathy, and nephropathy are infrequent reactions and are usually associated with high doses of parenteral penicillin.

HOW SUPPLIED: Pfizerpen VK (potassium phenoxymethyl penicillin) for Oral Solution. Each 5 ml. of reconstituted solution contains potassium phenoxymethyl penicillin equivalent to 125 mg. (200,000 units) or 250 mg. (400,000 units) of phenoxymethyl penicillin.

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250 mg. bottles of 100 ml. and 150 ml.

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500 mg. bottles of 100.

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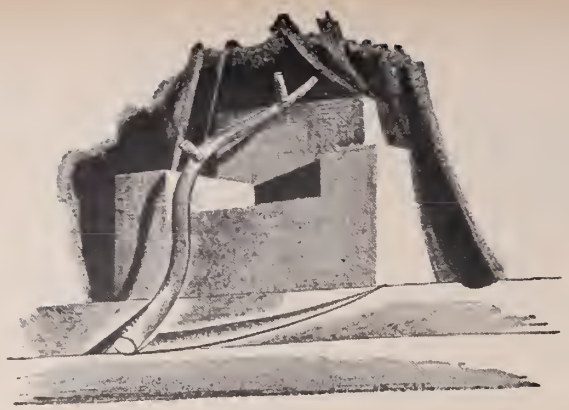
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OBITUSSIN A-C®	●	●			
OBITUSSIN-DM®	●		●		●
OBITUSSIN-PE®				●	●
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In Memoriam

We begin to die as soon as we are born, and the end is linked to the beginning.—Manilius

JOEL L. E. PETERSON, M.D.

Dr. Joel L. E. Peterson, 75, St. Paul physician, died October 5. A native of Wilton, North Dakota, Dr. Peterson had lived in the St. Paul area for the past 43 years. A graduate of Gustavus Adolphus College and the University of Minnesota Medical School, he had been in private practice for 41 years.

Dr. Peterson was a member of the Ramsey County Medical Society and the American Medical Association and a Life Member of the Minnesota State Medical Association.

He is survived by a daughter, Mrs. Roy Gustafson, and two sons, Orville J. and Fred J.

HENRY B. TROOST, M.D.

Dr. Henry B. Troost, 66, Mankato internist, died July 12. Born in Mankato, Dr. Troost attended the University of Minnesota Medical School.

He was on the staff of St. Joseph's and Immanuel Hospitals in Mankato and a member of the Blue Earth County Medical Society and the American Medical Association. Dr. Troost was also an Associate Member of the Minnesota State Medical Association.

He is survived by his wife, Betty.

ELMER W. LIPPMANN, M.D.

Dr. Elmer W. Lippmann, 67, Hutchinson physician, died July 23. Born in Gibbon, Minnesota, Dr. Lippmann had attended the University of Minnesota Medical School.

He was a member and a past president of the McLeod County Medical Society, a member of the American Medical Association and the Minnesota State Medical Association.

Dr. Lippman is survived by his wife, Rose, and a son.

WILLIAM A. BRAND, M.D.

Dr. William A. Brand, 95, Redwood physician for 70 years, died September 26. A University of Minnesota Medical School graduate, Dr. Brand continued working until a month before his death.

He was a member of the Kandiyohi-Swift-Meeker County Medical Society and the American Medical Assoication and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Brand is survived by his wife, Bernese, and three grandchildren.

SAMUEL T. SANDELL, M.D.

Dr. Samuel T. Sandell, 63, Nopeming, died last February 11. A native of Eveleth, he was a 1937 graduate of the University of Minnesota Medical School. He served on the staff of Glen Lake Sanatorium, Minneapolis, from 1939 to 1944; on the staff of Nopeming Sanatorium from 1944 to 1954, and as the medical director of Middle River Sanatorium, Hawthorne.

He was a member of the American Medical Association, St. Louis County Medical Society, the American Thoracic Society, American College of Chest Physicians and the Minnesota State Medical Association.

Dr. Sandell is survived by his wife, Christine, a daughter, and a son, Dr. Emmett G. Proctor.

CLIFFORD O. ERICKSON, M.D.

Dr. Clifford O. Erickson, 63, one of the founding partners of the Minneapolis Clinic of Phychiatry and Neurology, died October 25. He had been a psychiatrist with the state hospital system from 1937 to 1946, serving in Fergus Falls and Rochester, and then was in private practice in Minneapolis until he helped found the clinic. He was a past chief of psychiatry of the clinic.

Dr. Erickson was a past president of the Minnesota Psychiatrict Society, a clinical associate professor of psychiatry at the University of Minnesota, and a member of the American Medical Association, the Hennepin County Medical Society and the Minnesota State Medical Association.

He is survived by his wife, Bernice, a son, Bruce, and a daughter, Lois.

NORBERT J. KULZER, M.D.

Dr. Norbert Kulzer, 65, Hastings physician, died October 21, in the snow-covered Missionary Ridge area of Durango, Colorado. He was on a hunting trip.

He was a member of the American Medical Association, the Washington County Medical Society and the Minnesota State Medical Association.

Dr. Kulzer is survived by his wife, Margaret, and two sons.

MANLEY F. FELLOWS, M.D.

Dr. M. Fording Fellows, 69, Duluth ophthalmologist, died November 24. He had practiced medicine in Duluth for about 40 years. Born in Belvidere, Illinois, Dr. Fellows graduated from the University of Illinois Medical School and did graduate work in ophthalmology at the University of Minnesota.

He was a member of the St. Louis County Medical Society, the Minnesota State Medical Association, American Medical Association, a fellow of the American Academy of Ophthalmology and Otolaryngology and a member of the Minnesota Academy of Ophthalmology and Otolaryngology.

Dr. Fellows is survived by his wife, Pauline, a son and a daughter.

Legislative

Medicredit

And Other National Health Insurance Proposals

SUBTLY BUT NOTICEABLY, many Americans from various strata of society and economic classes are adopting the idea that good health care like good education ought to be a fundamental right of citizenship.

In a policy statement adopted by the House of Delegates in December, 1966, the American Medical Association stated, "It is a basic right of every citizen to have available to him adequate health care; it is a basic right of every citizen to have a free choice of physician and institution . . . the medical profession using all means at its disposal, should endeavor to make good medical care available to each person. . . . Health care for the poor should not be disassociated from, but rather should be a vital part of the overall health care system."

In an attempt to meet these stated objectives the American Medical Association had introduced into the 92nd Congress HR 4960, the Fulton-Broyhill Bill, known as the Health Care Insurance Act and commonly called MEDICREDIT. The companion bill has been introduced in the U.S. Senate as S. 987 by Senator Clifford Hansen of Wyoming.

The American Medical Association's Medicredit bill is a federally-financed program providing protection against ordinary and catastrophic expenses of illness and accident for all individuals and families, regardless of income levels. It is a system of voluntary comprehensive health insurance covering all persons under 65. Medicare would continue for persons 65 or older.

Under the basic portion of Medicredit, the government would pay 100% of the insurance premium for individuals and families whose incomes for a taxable year would not produce any income tax. For others, the government would give partial support based on a scale from 99% to 10%. Individuals or families with a low income tax would receive more financial assistance than those with a higher income tax. As the amount of income tax rises, federal assistance would decrease. Medicredit is, therefore, designed to give maximum help to those who need it most, and minimum help to those who are best able to pay their own way.

Under the catastrophic portion of Medicredit, the government would pay the entire premium for catastrophic health insurance without regard to income level.

A person or family eligible for full payment of the basic coverage premium by the government would receive a certificate to obtain qualified health care insurance. Those who receive partial assistance could choose between a credit against income tax or a certificate for the amount of the assistance. The insurance carrier who receives these certificates would present them to the government for redemption.

In order to be included in the Medicredit program, an insurance plan would have to meet all state regulations, provide certain minimum coverage, make coverage available without restriction on pre-existing health conditions and guarantee annual renewal. An assigned risk insurance pool among the insurance carriers would be utilized when appropriate.

Medical care under a qualified basic plan would include all medical services (diagnostic, therapeutic, and preventative) provided by or under the direction of a doctor of medicine or a doctor of osteopathy. Basic benefits would provide 60 days of inpatient hospital care in a 12-month policy period. Within the 60-day limit, two days in an extended care unit would count as only one day.

Such services would consist of the diagnosis or treatment of illness, psychiatric care, well baby care, inoculation and immunization, examination, consultation, and services for pregnancy and any of its complications. Cosmetic surgery would be provided when necessary to correct deformities sustained through injury or illness. Additional benefits would include emergency or outpatient hospital services, ambulance services, and dental or oral surgery when related to fractures of the jaw.

The basic coverage of any policy purchased under Medicredit would contain a set of deductibles or an amount the patient pays before the program itself begins to meet expenses. These deductibles are computed as follows: $50.00 for hospital stay; 20% of the first $500.00 of medical expenses; and 20% of the first $500.00 of emergency or outpatient expenses.

The catastrophic protection would pay expenses for services in a hospital in excess of the 60-day basic coverage limit as well as an additional 30-day treatment in an extended care facility. Unlimited physician services would continue to be provided under the basic coverage. If the basic benefits should become exhausted, a set of deductibles would come into play under the catastrophic coverage. The amount of the deductible would be based on the individual's or family's taxable income remaining after allowable deductions and personal exemptions; 10% on the first $4,000; 15% on the next $3,000, and 20% thereafter. This deductible would be eliminated in some cases and reduced in every case by the deductibles paid under basic coverage. The cost of Medicredit has been estimated to be $14.5 billion for the first year.

At least 40 other bills containing combinations of the words "national", "health", and "insurance" will compete with the AMA's Medicredit proposal for congressional consideration this session.

The bills that have received the most support, in brief, are these:

The National Health Insurance Partnership Act

Introduced by the Nixon administration, this plan would require employers to provide health insurance with a uniform level of benefits to all employees, while a companion family health insurance plan would use general tax revenues to underwrite policies for low income families with children replacing that part of the Medicaid program. Under this program, employees could elect to be enrolled in health maintenance organizations, the development of which will be encouraged, rather than receive the basic coverage through private insurance carriers. Estimated cost of this program would be $12.4 billion per year.

The Health Security Act

Sponsored by Senator Kennedy with the backing of organized labor, this proposal would pay almost all the health expenses of all Americans through a combination of general tax revenues and payroll levies. Allotments would be made to local regions for payments to physicians by salary, special stipend, capitation fee for service or other methods. Fee schedules would be established and all physician payments would be made directly by the government. The Social Security Administration estimates that the Kennedy plan would cost about $77 billion annually, amounting to a yearly tax impact of $1,271 on a typical family; present health programs cost the average household $405 yearly.

National Health Care Act

Backed by the Health Insurance Association of America, this bill would provide both tax credits and policies for the poor, but would have the states play a major role in the program's administration. This bill also has provisions relating to the supply of health manpower, the promotion of ambulatory care, health planning, and cost and quality. The HIAA plan is estimated to cost $15 billion annually.

National Health Insurance and Health Service Improvement Act

Introduced by Senator Javits, the plan would provide a system of national health insurance to be implemented by expanding the present Medicare program to include all individuals. SSA estimates the Javits bill would cost $66.4 billion in 1975 when fully implemented.

The Catastrophic Illness Insurance Act

Sponsored by Senator Long, the bill would amend the Social Security Act to provide coverage for the catastrophic cost of protracted or severe illness. The program would be financed by a gradual increase in the Social Security tax rate.

The Extra Care Plan

Introduced by Representative Durwood Hall, a physician, the Extra Care Plan would establish a program of basic health care protection for the medically indigent and catastrophic illness insurance for everyone. Complete cost estimates on the Long and Hall bills are not available.

Congressman Wilbur Mills, chairman of the House Ways and Means Committee, has indicated he will also introduce a compromise type bill for consideration by his committee.

Congressional hearings on these and other proposals will continue to play to packed houses as national health insurance will figure prominently in the 1972 election year issues. Medicredit has, however, engendered more congressional support than any of the proposals introduced to date.

One hundred and sixty congressmen are currently listed as sponsors of the AMA's Medicredit bill including Minnesota's Congressmen Ancher Nelsen and John Zwach, Senator Clifford Hansen, in testimony before the House Ways and Means Committee, noted that Medicredit "is a bill which will work, a bill which makes sense and an approach which the American people will support and can afford."

Medicredit does not require restructuring the entire health care system, which provides care very well for the vast majority of Americans. Some of the other programs before Congress would dismantle what now exists and rebuild it along untried lines. It does not hold up group practice or any other form of medical practice as the best or only effective system of patient care. Medicredit permits flexibility and innovation in developing new more efficient ways to take care of people. It permits free choice of physician by every patient and free choice by every physician as to how he will conduct his practice.

Finally, Medicredit does not obligate the government—the nation's taxpayers—to pay for care of people who can afford to handle most of their medical problems themselves.

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WANTED NOW: General Practitioner and a Surgeon to join our three-doctor Clinic in Northwest Wisconsin Resort, Forest and Retirement Area Town of 2,400 with a patient population of 25,000. Fully equipped modern Clinic building, with new accredited 50-bed Hospital and 50-bed extended care nursing home. Deer, ducks, partridge and fish 5 minutes away. Generous salary commensurate with training and experience the first year, then full partnership. Brochure with maps and photos upon request. Call collect or write L. J. Olson, M. D., Spooner Clinic Ltd., Spooner, Wisconsin 54801, telephone 715-635-2151.

AVAILABLE—Young married G.P. with some surgical experience. Deferment not needed. Write Minnesota Medicine, 462, 375 Jackson St., St. Paul 55101.

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LOCUM TENENS WANTED for July and August, 1972 in Northwest Wisconsin Resort Area Incorporated Practice. Pay $2,000 per month. Will welcome applicant for any other month. Permanent association could result. Send profile to Box 463 Classified Advertisements, c/o Minnesota Medicine, 375 Jackson, St. Paul, Minn. 55101.

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3. American Druggist BLUEBOOK, March, 1971.

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Precautions: As with other thyroid preparations, an overdosage may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Disease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg. SYNTHROID (sodium levothyroxine) TABLET is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose, preferably after breakfast. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily, and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurements about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, N.F., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) **for Injection** may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

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New Orleans Graduate Medical Assembly

When The New Orleans Graduate Medical Assembly convenes again this year, it will be for their 35th annual meeting, to be held March 6-9, 1972 at The Fairmont Roosevelt Hotel. Twenty distinguished speakers, well-known for their various specialties, have been selected to report on medical advancements in their areas. Medical motion pictures, round-table luncheons, a clinicopathologic conference and entertainment for wives will add interest to the program, and a special pre-meeting Symposium by Lederle Laboratories is planned for Sunday March 5th entitled "Our Polluted Environment—Its Problems for the Clinician."

This program is acceptable for twenty-two (22) prescribed hours and eight (8) elective hours by the American Academy of Family Physicians. For further information write to The New Orleans Graduate Medical Assembly, 1430 Tulane Ave., New Orleans, La. 70112.

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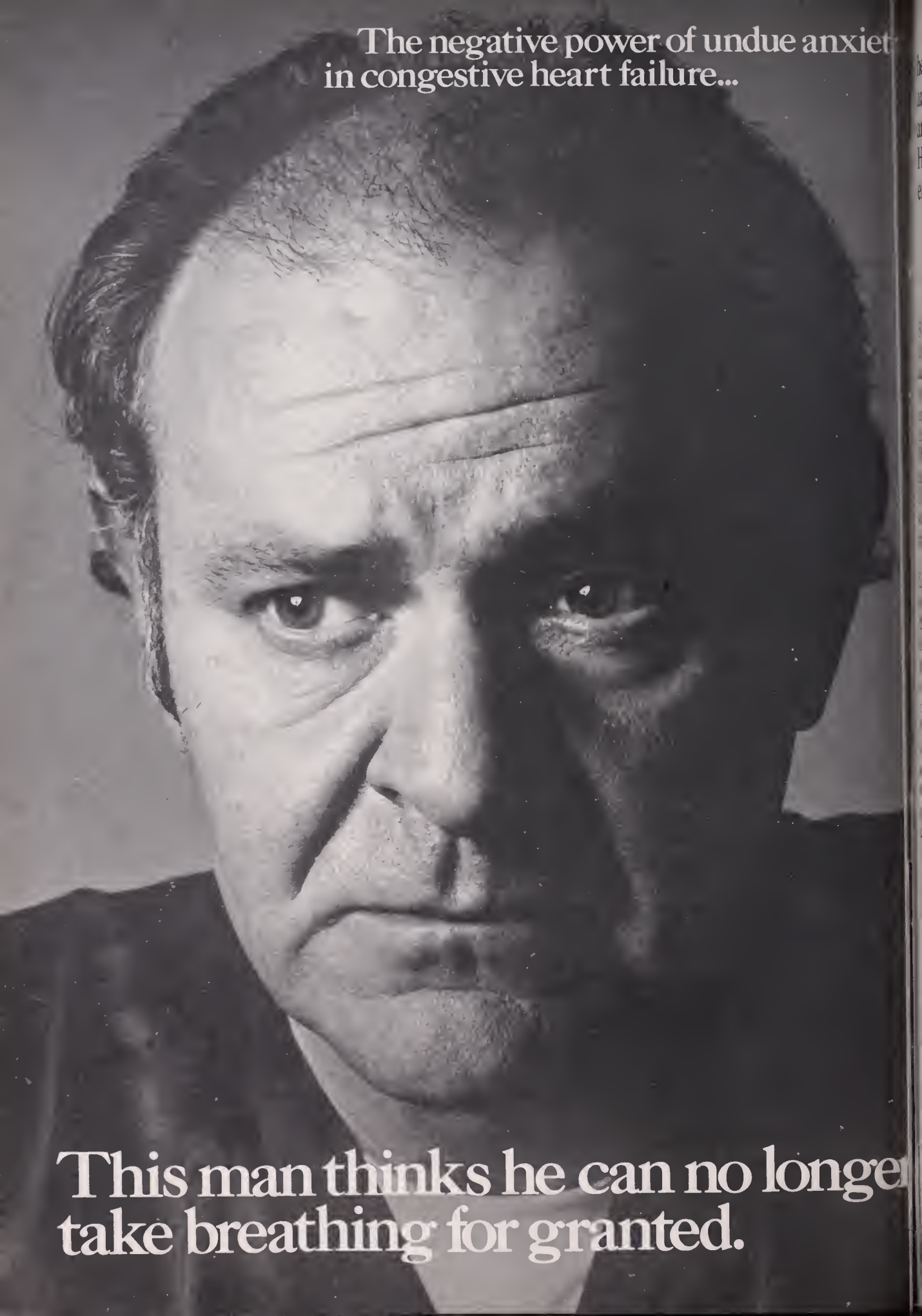
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Robert L. Wilder, M.D.

MARCH, 1972


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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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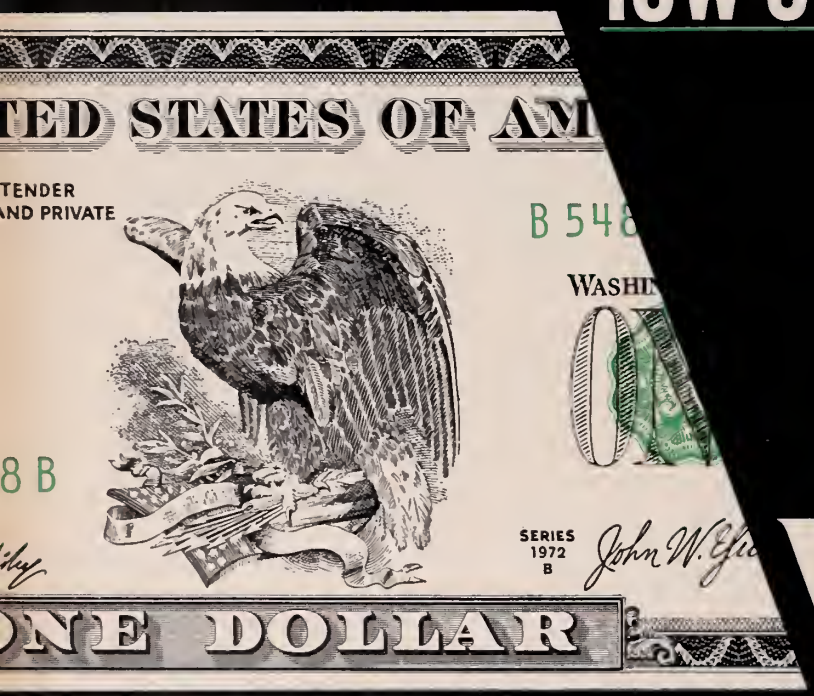
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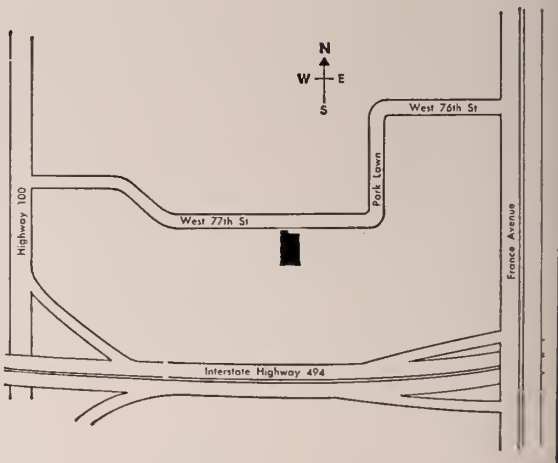
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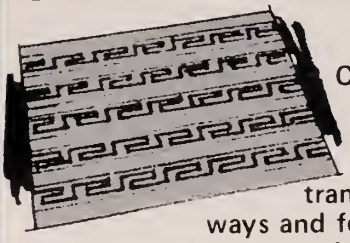
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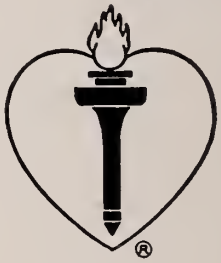
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President's Letter

Responsibility for Rising Health Care Costs*

WHEN WE SPEAK of health care costs, we must be certain to define what we mean. Many people confuse health care costs with medical care costs. Health care involves doctor services, hospitalization, nursing home care, pharmaceuticals, ambulance service, to name a few. Last year the cost for medical care, (physician services) amounted to approximately 12-17% of the health care costs, depending on the area in the United States. Consequently, the "doctor bill" is a small fraction of the overall health care costs. We, the physicians, have a definite responsibility to help control health care costs, and this is being done through utilization review committees in which the physicians donates time to participate in the activities of these committees. These committees' functions are to see that hospitalization costs, which account for approximately 50-55% of the health care dollar, are kept to a minimum while continuing to preserve quality care for the patient.

The patient, however has just as much responsibility in controlling the cost of health care as does the physician. Last year, it was estimated that the American people spent at least $2,000,000,000 for quackery, more than all the money spent on health education. In this modern day, people still spend money on worthless and sometimes harmful gadgets ranging from a copper bracelet to the Rainbow pill for dieting. Millions are spent on unnecessary frills such as health foods, reducing aids, patent medicine and other non-prescription items which cost the American public more than all the prescription drugs put together.

Think of the enormous savings that would occur if the nation could reduce accidents. In 1969, 49,000,000 people were injured; 20,000,000 at home, 9,000,000 at work, 3,500,000 on highways and 15,000,000 in non-moving motor vehicle accidents. Of the 49,000,000 accidents, 11,000,000 were bed disabling. The cost of medical and hospital care alone for these injuries was $3,000,000,000. Nearly all of this cost was preventable. Therefore, the patient does have a real stake in controlling costs of health care.

What about the effects of alcohol? There are 60,000,000 users of alcohol in this country, which includes approximately 10,000,000 alcoholics. Medical care for these alcoholics is part of the medical care that is called too expensive. This alcohol problem, too, can be reduced.

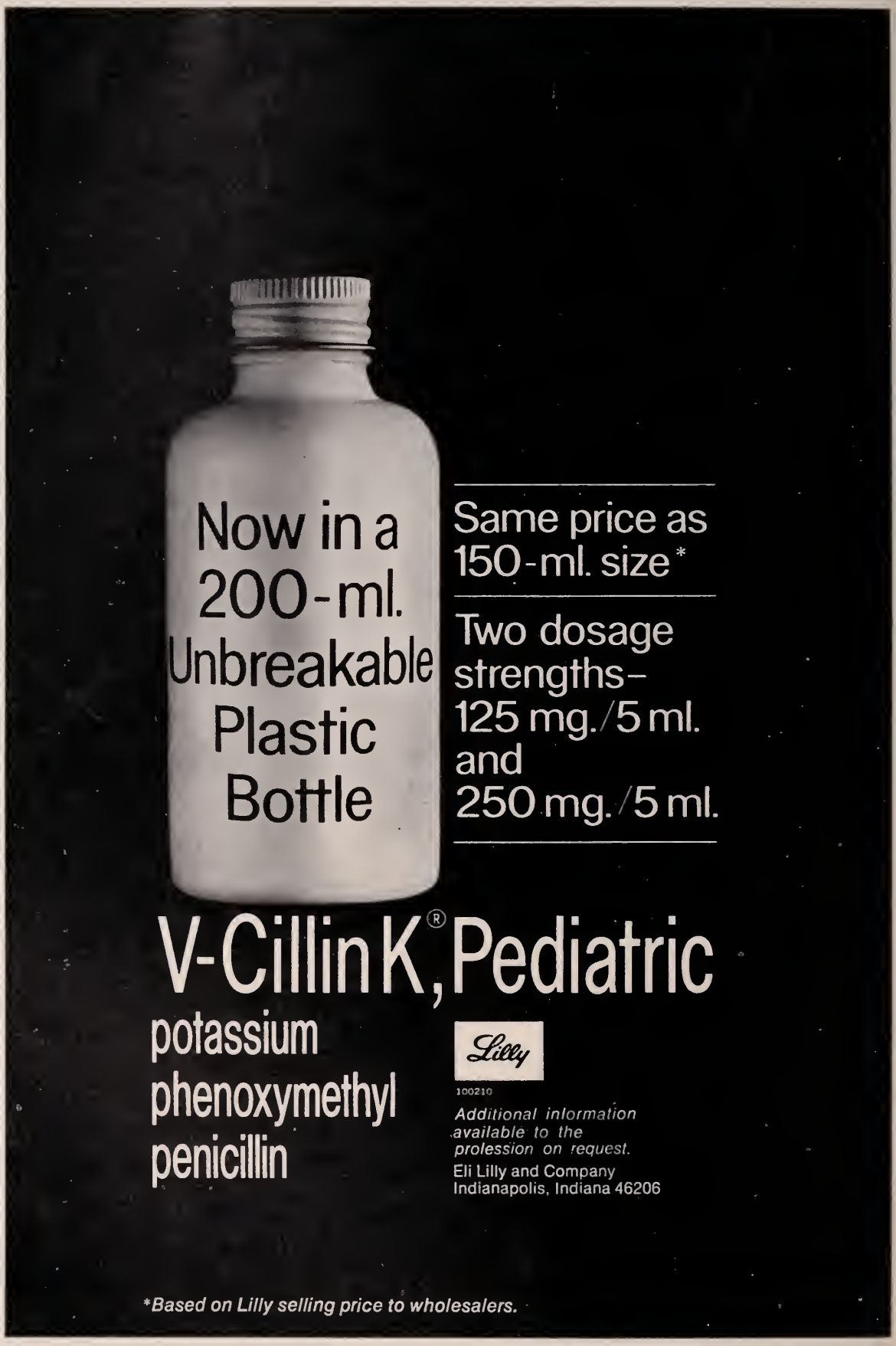
What about the average adult who over eats, does not exercise, smokes too much and does not get enough rest. How much does this self abuse add to the cost of health care in treating hypertension, cancer of the lung, arteriosclerosis, diabetes and strokes? It might be safe to say that half the cost of health care is preventable in this country. The doctors of the nation have been urging the American public for years, to use a little common sense and follow some simple rules to maintain good health.

The responsibility for preventing rising health care costs belong to all of us. The doctors of America accept this challenge, but we must also have responsible action on the part of the American public to be successful in controlling these costs.

Robert T. Kelly

President
Minnesota State Medical Association

*Statistics taken from article written by Jack Schreiber, M.D., Canfield, Ohio, in Ohio State Medical Journal, June, 1971, page 492; July, 1971, page 574 and August, 1971, page 704.


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Cancer of the Liver

Intra-Arterial Infusion

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THE RESPONSE OF CARCINOMAS to specific antitumor chemotherapeutic agents is usually dose-dependent. For neoplasms limited to a specific organ, intravenous or intramuscular therapy results in a large percentage of the dose being expended on normal tissues with a relatively small amount actually reaching the tumor. The toxicity of the agent on normal tissues is a limiting factor in the total allowable amount of drug that can be administered. Injection of an agent directly into the artery supplying the tumor provides a higher concentration in the tumor, a possible greater antitumor effect, and less toxicity to normal tissues. This concept of intra-arterial administration of anti-neoplastic drugs was introduced by Klopp in 1955 for the treatment of head and neck tumors.[1]

Radiotherapy and systemic chemotherapy have proved of limited practical value for the treatment of extensive metastatic and primary cancers involving the liver. The results of surgery, in the treatment of primary biliary and pancreatic carcinomas, are discouraging, since only 20% of these tumors are resectable,[2,3] and the use of radiation or systemic chemotherapy adds little to the management of these patients.[2]

The demonstration by Bierman[4] that the blood supply to normal liver is derived mainly from the portal vein (80-95 per cent), while the blood supply to developing intrahepatic tumors is derived mainly from the hepatic artery and its branches (85 per cent), established the rationale for the trial of intra-arterial chemotherapy for neoplasms in the liver.

Selective catheterization of the desired artery may be accomplished under direct vision by introducing the catheter through a collateral branch,[5,6,7] or the catheter may be introduced percutaneously through a brachial or femoral artery and then advanced under fluoroscopy into the desired artery.[8]

Administration of the fluorinated pyrimidines, 5-fuorouracil (5-FU) and 5-fluoro-2′-deoxyuridine (FUDR), via the celiac or hepatic arteries delivers a higher drug concentration into the tumor than into normal hepatic tissue.[6,9,10] Since these drugs are metabolized in the liver their systemic toxicity is reduced when they are delivered directly through the celiac or hepatic arteries;[8,10] yet they still induce an antitumor effect.[5,7,8,10]

Method

The infusion of 5-FU via the celiac or hepatic artery after percutaneous catheterization of the femoral artery and the use of the Fenwald closed system has been used in 51 patients with cancers involving the liver.

Preliminary Procedure

Prior to catheterization the following studies were obtained: hemogram and platelet count, prothrombin time, plasma thromboplastin time, alkaline phosphatase, SGOT, LDH and bilirubin. Every three days during the infusion period the alkaline phosphatase, SGOT, and LDH were determined and a three-fold increase in any of these enzymes from the base-line values constituted an indication to discontinue the infusion. The position of the catheter was checked flouro-

TABLE 1
Distribution of Tumor Types of 51 Patients with Liver Metastases

Primary Site	Number of Patients
Biliary tract	11
Pancreas	4
Colorectal	15
Stomach	4
Duodenum	2
Carcinoid	1
Hepatoma	2
Breast	4
Ovary	2
Melanoma	2
Primary unknown	4

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scopically every three days, and repositioning of the catheter was carried out when necessary.

Evaluation Procedure

Stomatitis, diarrhea, abdominal pain, or bleeding were the toxic manifestations used as indications to discontinue treatment. An objective improvement of the cancer was considered when any two of the following occurred: *1.* Fifty percent decrease in palpable liver size. *2.* Decrease in the number and size of hepatic metastases as determined by radioactive technetium sulfur colloid (Tc 99) liver scan. *3.* A return to normal of the bilirubin, SGOT, and LDH.

Subjective improvement was gauged by pain control, improvement of appetite, and weight gain, as well as by the daily performance of the patient.

Results

Biliary Tract Cases

Eleven patients with inoperable carcinomas originating in the biliary tract and involving the liver were treated by intrahepatic infusion of 5-fluorouracil. Objective improvement occurred in six of the patients and their median survival from the beginning of the study was a little more than 24 months. Two of them are alive and free of detectable disease; one is alive but jaundice has recurred (Table 2). In all of these six patients external biliary drainage was removed when jaundice disappeared.

Five of the 11 patients in this group had neither objective nor subjective improvement following the first infusion cycle of 5-FU therapy. Four had primary tumors of the gallbladder, and one, a carcinoma of the ampulla of Vater. Their median survival after admission to the study was three months.

Four patients with inoperable pancreatic carcinoma involving the liver were treated. Three had a decrease in tumor size, disappearance of pain, and weight gain. The median duration of life from the first infusion cycle was 11 months. A total of nine infusion cycles were given to this gorup.

Recurrent Colorectal Tumors

Fifteen patients had recurrent colorectal tumors involving the liver; five from the rectum, four from the sigmoid colon, three from the transverse colon, and three from the cecum. A total of 35 infusion cycles were administered to this group.

Objective tumor regressions were observed in six patients who also had an increase in appetite with a weight increase of eight to 12 pounds. (Table 3). The median duration of life from inclusion to the study was 10 months as compared to a median survival of two months for the patients who did not respond to intrahepatic infusion. *However, the total survival from primary diagnosis was the same for both groups.*

Miscellaneous Malignancies

Patients with small bowel carcinoma, hepatoma, melanoma and adenocarcinoma of unknown origin involving the liver did not respond to 5-FU infusion.

Of the four patients with liver metastasis from carcinoma of the breast, two died of drug toxicity. At post-mortem there was histologic evidence of tumor necrosis secondary to treatment. Objective tumor regression lasting six months was observed

TABLE 2
Biliary Carcinomas; Objective Response.

Age	Sex	Primary tumor	Duration response, months	Survival, months from diagnosis
24	M	Intrahepatic duct (4)	13	26, alive and well
48	F	Extrahepatic ducts	36	38, alive and well
43	M	Extrahepatic ducts	8	12
59	F	Common	19	26, alive and well
76	M	Gallbladder	9	14
68	M	Ampulla	15	22

TABLE 3
Colorectal Tumors; Objective Response to Intrahepatic Infusion

				Survival (months)	
Age	Sex	Primary tumor	Duration of response (months)	From infusion	From primary diagnosis
56	M	Rectum	4	6	9
61	F	Rectum	6	8	14
49	F	Sigmoid	2	18	45
44	M	Hepatic flexure	8	13	21
56	M	Splenic flexure	12	12	12, alive
61	F	Cecum	4	6	50

in the other two patients.

Complications

Four deaths (7.5%) were ascribed to toxic effects of the treatment: two of them due to sepsis and intravascular coagulation, and two to severe gastrointestinal toxicity and sepsis.

Severe reversible stomatitis, diarrhea, and leukopenia were observed in two patients. Catheter thrombosis was noted in five patents (9.4%), and in 12 instances the catheter was displaced. In all instances replacement or repositioning of the catheter allowed the completion of the cycle.

Discussion

Intra-arterial infusion has provided a means to deliver a high concentration of 5-fluorouracil to metastatic tumors involving the liver in diseases where conventional intravenous administration of this agent has been relatively ineffective. Percutaneous placement of the catheter through the femoral route [7,10] or the transbrachial approach[3] has become a familiar technique for most diagnostic radiologists. The method as used in this study is inexpensive and safe, thus making this therapeutic approach easily accessible.

Intra-arterial infusion of 5-fluorouracil for the treatment of inoperable carcinoma of the biliary tract was effective in six of 11 patients with these malignancies. The median duration of objective improvement was a little more than 24 months of comfortable survival.

In the treatment of colorectal tumors involving the liver, intra-arterial infusion of 5-fluorouracil has been demonstrated by others to produce objective remissions. Wirtnen[8] reported a 60 per cent remission rate, Burrows[10] and Rochlin[5] observed objective regression in 59 and 45 per cent of their respective patients. Of our patients, six of 15 (40%) had a decrease in liver size lasting a median of 10 months.

When a diagnosis of metastatic carcinoma of the liver is established at the time of exploratory surgery the surgeon has the opportunity to select the appropriate artery in which to place a catheter, thus providing the patient with an opportunity for further selective chemotherapy. At the completion of the course of intra-arterial chemotherapy, the catheter is clamped off for 24 hours, after which it can be gently pulled out, without any subsequent bleeding.

Summary

Fifty-one patients with a variety of tumors involving the liver, treated by celiac or hepatic artery infusion of 5-fluorouracil, were sufficiently benefitted to make this therapy an effective means for the management of these diseases.

Percutaneous catheterization of the femoral artery and the use of the Fenwald closed system are simple, inexpensive, and safe. A catheter and Fenwald closed system should be available for appropriate positioning when surgical exploration for gastronintestinal malignancy is carried out. If there is liver involvement, direct visualization of the desired collateral will make the need for a second procedure, percutaneous catheterization, unnecessary.

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Urinary Tract Infections

Diagnosis, Bacteriology and Treatment

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CERTAIN BASIC PRINCIPLES regarding urinary tract infections should be kept in mind. Bladder urine is normally sterile, and the presence of bacteriuria at any point along the urinary tract up to the distal urethra constitutes a deviation from normal. The demonstration and quantitation of bacteria by culture is fundamental in establishing the diagnosis of urinary tract infections. There are two major steps in arriving at an estimate of bacterial numbers in a urinary specimen. Initially, the specimen must be properly obtained and secondly, it must be quickly transported to and appropriately handled by the laboratory. Antimicrobial therapy of urinary tract infections should be based upon a knowledge of the organism causing the infection and upon an understanding of the historical background of the infective process.

Specimen Collection

An accurate urine specimen can be obtained from a properly supervised clean catch mid-stream urine, urethral catheterization, or suprapubic bladder aspiration. However, when women are asked to obtain a clean catch urine by themselves, as few as 20% will be able to obtain sterile urines, and from 5-10% will actually have bacterial counts in excess of 100,000 organisms per ml in spite of sterile bladder urine.[1] These disturbing statistics, resulting from distal urethral contamination, are greatly improved when the clean catch mid-stream urine specimen is obtained under the close supervision and instruction from a competent nurse. The material in the Table is taken from the data of Dr. E. H. Kass and deals with the reliability of bacterial counts from clean catch urine cultures.[2] Only 50 to 75% of catheterized urine specimens in patients with known sterile bladder urine will be absolutely sterile.[3,4,5] Multiplication of bacterial numbers may occur as often as every 20-30 minutes unless the urine specimen is cultured without delay, or is properly refrigerated.

Even very low counts of bacteria may be important in patients who are being treated with antimicrobial therapy, especially if the organism cultured is in pure culture or is the organism present in the pretreatment cultures.

Office Bacteriology

For a very fine review of the office bacteriology of urine specimens, the reader is referred to the article by Stamey.[6]

Simple methods of culturing urine utilize spoon or dip-slide devices containing sterile media.[7,8] These commercially available devices are dipped into the urine and then incubated and observed for numbers of bacterial colonies and for growth characteristics. Our experience with these devices indicates that they can be used with good accuracy on freshly obtained specimens, and are especially helpful in routine screening.

For the physician who does not have ready access to a competent laboratory, transit of the urine specimen from his office to the laboratory may cause just the delay necessary to allow organism multiplication. Bacteriology done in a small laboratory within the physician's office setting can be very satisfactory and more economical for the patient. Bacteriology for urine specimens can be done rapidly and accurately using a calibrated innoculating loop and a blood agar plate and a selective differential media plate (MacConkey's or Eosin-Methylene Blue). A small incubator costs as little as $75 and takes up relatively little space. Identification of organisms, if necessary, can be readily accomplished by using the Enterotube (Roche)[9].

TABLE
Reliability of Bacterial Count from Clean Catch Urine Cultures.[2]

1st Count	Chance of 2nd count exceeding 100,000/ml (critical level)
10,000 or less	1%
100,000 or more	85%
1,000,000 or more	96%

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Patho-Tec (General Diagnostics)[10] or Analytab Systems (Analytab Products, Inc.).[11] Identification of organisms is particularly useful in delineating the epidemiology of recurrent bacteriuria. Antibiotic sensitivity testing can be readily and practically accomplished by using the high potency single antibiotic disc technique.[12-15]

Antimicrobial Therapy

Uncomplicated Acute Cystitis

Infections in this category will not infrequently resolve spontaneously. Treatment is usually based on the realization that the causative organism is most often a broadly sensitive *E. coli,* especially if the infection is a first urinary tract infection. It must be stressed that while therapy may be successful in as many as 95% of patients, one cannot rely solely upon the disappearance of symptoms to judge the effectiveness of therapy, as this may not be a true indicator of bacterial eradication. In cystitis, the presence of an antimicrobial agent for a period of one hour will clear most infections limited to the lower urinary tract[16], and one or two adequate doses of an agent such as kanamycin or cephaloridine will usually result in a bacteriological cure.[17] In truth, this ability to clear cystitis with seeming ease can be a helpful diagnostic tool in differentiating upper from lower urinary tract infection. The best approach then, to patient therapy, whether it be in uncomplicated or recurrent cystitis, would be to repeat a urine culture two to four days after beginning treatment, and thereafter two or three cultures at least should be spaced over the period of six to 12 months.

Since the organism being treated in the vast majority of cases of acute cystitis is a susceptible *E. coli* one has wide latitude in choosing an antimicrobial agent. There is no convincing evidence that any one antimicrobial agent is better than another, be they bactericidal or bacteristatic as long as the result of that therapy is a sterile urine. Sulfonamides are usually adequate, inexpensive and well tolerated. Other agents which may be considered would include nitrofurantoin, ampicillin, an oral cephalosporin, naladixic acid or, in adults, tetracyclines.

Acute Pyelonephritis

Therapy in pyelonephritis will in part be dependent upon the severity of the acute infection, and will frequently depend on whether or not the patient is hospitalized. In the more severe episodes, especially if vomiting is a part of the patient's clinical picture, parenteral medication is indicated. In recurrent or chronic situations with an acute episode, one should realize that other organisms such as *Klebsiella, Proteus,* or *Pseudomonas* may be involved. Our recommendation would be that in a severe episode of pyelonephritis one institute therapy with kanamycin, gentamicin or polymyxin B after obtaining an initial impression of the presence of gram negative organisms by the gram stain. A word of caution is indicated here since one can have a negative gram stain in the presence of subsequent culturally proven bacteriuria.[18] This can be the situation in twenty percent of instances with 100,000 organisms per ml, although the gram stain correlation is much better if there are over 1,000,000 organisms per ml. Culture results will furnish an accurate organism diagnosis and allow for revision of therapy if it is indicated. One should remember that enterococci and staphylococci can cause urinary tract infection and should be considered among etiologic possibilities. Treatment of acute pyelonephritis is probably best maintained for 10-14 days. Follow-up cultures at decreasing intervals for a year or more are necessary to insure that the patient remains infection free.

Complicated Urinary Tract Infections

Females having complicated urinary tract infections are those who frequently require urologic surgical procedures for *basic anatomic abnormalities* and/or urinary calculi.

Patients with *neurogenic bladders* (bladder paralysis) are also considered to have complicated urinary tract infections, and these patients are difficult to maintain infection free because of their difficulty in emptying adequately. Consideration should be given to surgical diversion in order to prevent renal deterioration secondary to persistent urinary infections. Our data[19] has shown that, in *intestinal urinary diversion* patients, 50% of cultures had greater than 100,000 organisms per ml, and 70% had some bacteria. No patient always had a sterile urine culture. Bacteriuria in these patients is largely asymptomatic. Studies are currently underway to determine the importance of bacteriuria in this patient population.

The possible high incidence of bacteriuria in infants[20] should also be briefly mentioned in the category of complicated urinary infections, but will not be discussed here.

Asymptomatic Bacteriuria

Kunin[21,22] has demonstrated that bacteriuria ex-

ists in about 1.48% of school girls, with two-thirds having no symtoms referable to the urinary tract. His figures indicate that at least 5% of girls will acquire bacteriuria during the elementary and high school years. This incidence increases with age until it is estimated that 10% of adult women over age 60 have bacteriuria. The majority of this population will be asymptomatic, and these patients with asymptomatic bacteriuria constitute the largest group of patients with urinary infections.[23] The presence of bacteriuria should be established by a minimum of two consecutive cultures. Specific antimicrobial therapy is based upon the results of sensitivity testing since organisms may be of a more resistant nature. The treatment is most often with an oral antimicrobial agent, and the principle of using the least toxic, most economical agent to which the organism is sensitive is usually wisest. These patients are often difficult to treat in that the bacteriuria often recurs. Recurrence in females is an indication for a urologic work-up, and for longer duration specific therapy. In the male patient and in the female pediatric patient, one considers a urologic work-up upon initially documenting the diagnosis of bacteriuria.

Recurrent Bacteriuria

A relapse has been defined as being a recurrence due to the same biotype of bacteria, whereas a re-infection is a recurrence with a new strain of the same or another species. Since at least one-half of patients with acute urinary infections and asymptomatic bacteriuria will have a recurrence after a successful course of antimicrobial therapy, it is mandatory that one know the *in vitro* susceptibility of the pathogen involved as this may well be the deciding factor in the selection of an antimicrobial agent and in determining the duration of the therapy. We have found the use of the methenamine salts, methenamine mandelate[24] and methenamine hippurate[25,26] along with urinary acidification to be effective in preventing repeated infection. These patients are advised to maintain adequate hydration, to void frequently, to maintain proper hygiene, and to avoid tub baths.

Some women may experience repeated episodes of urinary tract infection following sexual intercourse. These patients should be encouraged to maintain proper hydration, to void after intercourse, and to take one dose of an antimicrobial agent. Stamey[1] advises oral penicillin-G, 250 or 500 mg as being effective. Ronald advocates sulfisoxazole 500 mg or nitrofurantoin 50 mg as being appropriate.[23]

When the patient has well documented, recurrent urinary tract infections the recurrence rate following conventional therapy approximates 80%.[27] Thus, this group poses "the most severe therapeutic challenge."

Infection or Bacteriuria in the Male

Almost all males who develop a urinary infection or bacteriuria have an underlying urologic problem and deserve a urologic evaluation. The younger male population almost always have problems which should be approached surgically. In the older male population the underlying problem is most often either prostatic hypertrophy or calculi, with a surgical approach an advisable concommitant to antimicrobial therapy. Therapy should be dictated by sensitivity tests. There is a group of male patients who have chronic prostatic seeding of bacteria into the urinary tract. Eradication can be very difficult in certain of these individuals, and it may be best to maintain specific antimicrobial therapy in reduced dosage in order to keep bladder urine sterile and the patient symptom free.[28]

Urinary Infection in the Catheterized Patient

Prevention of infection is the best approach in these patients. Strict adherence to technique in inserting the catheter is a first step.[29,30] Subsequent use of either a closed urinary drainage system[31,32], or a system employing a continuous antimicrobial irrigation system[33,34] is strongly advocated in decreasing the incidence of catheter-induced infection. Neither of these systems is effective in patients with pre-existing bacteriuria. Systemic use of antibiotics will not prevent catheter-induced infection, and, indeed, may lead to infection with *Pseudomonas* or other relatively resistant organisms. The attempt to eradicate infection without catheter removal is very difficult at best.

Summary

To demonstrate the presence of bacteriuria one must insure that proper culturing is carried out, that the refrigerated specimen is transported to the laboratory without delay, and that quantitative bacteriology is carried out. If an organism is present in the urine, there should be either sufficient patient symptoms, or an appropriate repeat culture to confirm that infection exists. Antimicrobial

therapy is then indicated. The agent used is determined by the consideration of the location and severity of the condition being treated, the in vitro sensitivity pattern of the organism isolated, the renal and liver function of the patient, and the pharmacological and economic factors of the possible effective agents. The duration of therapy depends on the nature of the infection and the existence of history of recent prior infections.

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Gynecologic Operations for Sterilization

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THE DESIRABILITY of sterilizing certain women is a universally accepted fact. Frequently the desirability becomes a necessity for the preservation of the health and even the life of the patient. The indications for sterilization are numerous, and certainly many of them are debatable; but most of the arguments are based on religious or moral views. It is assumed that even the most conservative physician will occasionally be faced with the necessity of sterilizing a woman. This review is not intended to deal with the many indications for or the many philosophic aspects of sterilization.

History

Sterilization of the female has been of interest to the medical profession since it first was contemplated by Hippocrates as a means of eliminating hereditary perpetuation of the insane.[1] The earliest operations were on the ovaries by oophorectomy. Von Blundell is credited with the initial written suggestion of tubal sterilization, published in 1834.[1] He suggested total resection, but he wrote that simple division might successfully prevent pregnancy. Among other earlier procedures was burying the ovaries in pockets in the broad ligaments[2]; this had the possibility of restoring fertility at a later date, if desired, by replacing the ovaries in the abdominal cavity.

In 1850, Froriep proposed the creation of a chemical slough stricture in the uterine corners to prevent pregnancy and suggested silver nitrate for that purpose.[2] Koch in 1878 used a galvanocautery to create such a slough.[3]

The same principle was revived by Dickinson in 1916, and in 1929 he described his use of the hysteroscope to visualize the tubal openings.[2] In 1934 Hyams[4] described his technique of coagulating the tubal ostia and mentioned the use of a fluoroscope for direct visualization.

Rein was the first, in 1876, to propose hysterectomy for the purpose of sterilization.[2] Having relieved a patient of sterility by removing a cervical polyp, Kock suggested establishing a cervical polyp to interfere with conception.[2] Pincus performed atmocausis (distruction of the endometrium by steam).[2] This was especially advocated by Cramer in 1904, but he reported bad results and severe colic, and sometimes a hysterectomy had to be done for complications.[3]

Between 1880 and 1910 various procedures were carried out, with uniformly poor results. An extensive report by Nurnberger in 1917 described 36 methods of tubal sterilization. He concluded that salpingectomy or cornual resection was the best.[1]

In 1919 Madlener[5] described his technique of crushing the tubes. Williams,[6] in 1921, described the utilization of cesarean hysterectomy for preventing further pregnancies. In 1924 Irving[7] described his method of tubal sterilization, and in 1930 Bishop and Nelms[8] described the Pomeroy procedure. Postpartum tubal sterilization was popularized in this country by Adair and Brown[9] who performed the operation within 24 hours after delivery. The only new procedure which has received much attention in the last decade is the one described by Uchida[10] in 1961.

Surgical Methods of Sterilization

In the restricted sense of the term, the sterilization of a woman refers to surgical procedures intended to prevent the union of spermatozoon and ovum.

Hysterectomy

The techniques for interval hysterectomy or cesarean hysterectomy will not be described here,

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but their advantages and disadvantages will be discussed below.

Salpingectomy

There are more than 100 variations of techniques for interruption of the continuity of the tubal lumen to prevent conception. Of these, only a few are now in common use. Nonpuerperal, interval tubal sterilization may be performed at any time, but the menstrual period and the immediate premenstrual and postmenstrual days should be avoided. When tubal sterilization is to be done in the puerperium, however, it should be performed as soon as possible and not later than 48 hours after delivery. After that time, increasing edema makes the operation more difficult, with higher incidences of hemorrhage, infection, and failures. The edema subsides by the seventh to the 10th day but by that time the involution of the uterus has rendered the tubes more inaccessible, thus making the operation unneccessarily extensive and risky. If the operation cannot be accomplished during the first 48 hours after delivery, it should be delayed until six to eight weeks later.

Complete Salpingectomy

This was recommended by some of the earlier writers as one of the safest operations for accomplishing sterility, at a time when surgeons were discouraged by the high failure rate of the then known procedures. However, the simpler partial salpingectomies give results essentially the same as those of complete salpingectomy.

Partial Salpingectomy and Tubal Ligation

In 1906 Friedemann described a method of sterilization in which the tube was crushed and then ligated with catgut[5]. Madlener[5], in 1919, described an operation with the same principle; instead of an absorbable ligature, however, he used cotton thread.

Madlener Operation

The tube is grasped with a thumb forceps in the middle or more lateral portion and is pulled up at an approximately 90° angle (Figure 1). With a Doyen intestinal clamp (which has a 9-mm crushing surface) the loop of the tube is crushed in the coronal plane, involving a part of the mesosal-

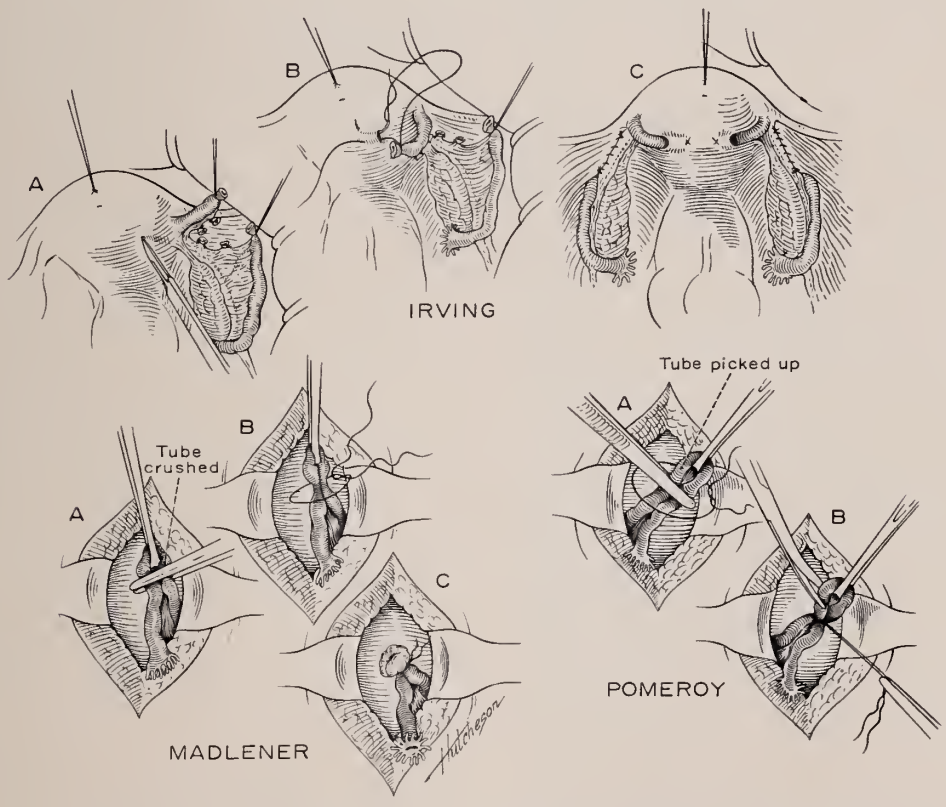


Fig. 1—Principles of Madlener, Irving, and Pomeroy procedures for tubal ligation. Note that in Pomeroy procedure loop is grasped with thumb forceps, not crushing clamp, to lead ligation. In Madlener technique, no tubal tissue is excised.

pinx. The crushing should be forceful enough so that the tissue becomes paper thin. The loop is then ligated with a thin cotton thread. The tissue should not be traumatized beyond the clean crushing.

In 1932 Madlener[11] reported a total of 166 cases over 22 years without a known failure. Von Waser reported one failure in 225 cases[12]. In 1933 Gianella, who introduced a modification by suturing the crushed tube beneath the round ligament, collected 604 cases with only one subsequent pregnancy[1]. The failure rate for this operation in the hands of many other surgeons increased over the next decades and, according to Garb[1], the overall failure rate is 1.44% in 7,829 cases.

Irving Operation

In this operation, described in 1924[7], the tube is elevated 1½ inches from its cornual insertion (Figure 1). The mesosalpinx beneath this point is pierced by a hemostat in an avascular area. The distal portion of the tube is ligated with 1-0 chromic catgut. Proximal to this a double suture ligature of the same material, mounted on a half-curved, round-pointed needle and knotted about three inches from its end, is tied around the tube which is then divided between the two ligatures. A stab wound is made in the myometrium at the uterine end of the tube. A sharp-pointed hemostat is then plunged into the uterine wall through this stab wound as far as its lock. Its tips are spread, thus making a pit. A grooved director is inserted in this pit as far as it will go, and the half-curved needle is passed along the director to the extreme depth of the pit and then brought out on the surface of the uterus. Traction on the ligature causes the tube to enter the pit for approximately ¾ inch. One strand of the double suture ligature is cut, a cross-stitch is made in the superficial portion of the uterine wall, and the free ends are tied, thus anchoring the tube deeply in the myometrium. The small wound at the point of the tube is closed with a figure-eight suture of chromic catgut to complete the operation.

From 1916 through 1949, 814 women were sterilized by this method at Boston Lying-In Hospital with no known failures[13]. A few failures have been reported, but there was no failure in the 1,056 cases collected by Garb[1]. The main disadtages of this operation are the amount of time it takes and the amount of bleeding it causes.

Pomeroy Operation

In 1930 Bishop and Nelms[8] described a method of sterilization which they said they had first seen performed by Ralph Pomeroy. Pomeroy had made no claim for originality but said that he had never seen it done before. In this procedure, a loop in the loose, middle portion of the tube is ligated with absorbable suture material and resected (Figure 1). Bishop and Nelms wrote, "We definitely do *not* crush the tube first . . . for the crushed tissue may open a way for fistula formation; we definitely do *not* use non-absorbable ligature material as that very material, we fear, might slough through and a fistula develop." They reported 100 cases without failure. Separation of the cut ends is considered an important point and can be achieved only by using an absorbable suture which dissolves quickly. In 1947 Nelms and Doyle[14] reported 404 cases with only one subsequent pregnancy.

In Lull and Mitchell's series[15], which extended over 25 years, there were 1,550 women, with four failures reported. Two were due to a wrong technique, but in the other two cases the Pomeroy technique had been followed explicitly. They emphasized that the loop should be made in the middle third of the tube because, if it is too close to an involuting uterus, the ligature might slip. The overall failure rate is reported by Garb[1] as 0.40% in 5,477 cases.

Uchida Operation

In 1961, a new technique of tubal sterilization was described[10] as used in nearly 5,000 cases without a failure. Through a small abdominal incision, the tube is delivered by a special hook (an Allis clamp serves as well). The serosal surface of the tube at about its midpoint is then dissected away from the muscular tube by means of subserosal injection of saline-epinephrine solution to produce considerable ballooning of the adjacent mesosalpinx. This produces local vascular spasm and neatly demonstrates avascular areas of the serosa. The latter is incised at such an area, and the muscular tube is delivered through the incision and divided. The proximal limb of the tube is stripped back and about 5 cm of it is cut off, to leave only a small stump. This is ligated with chromic catgut and allowed to fall back within the serosal balloon. A pursestring ligature of fine chromic catgut then gathers up the edges of the serosal incision and is

tied about the cut end of the distal limb of tube so that it projects into the abdominal cavity.

Vaginal Route

Smith and Symmonds[16] at the Mayo Clinic performed partial salpingectomy by the vaginal route in 161 patients. Sixty to 80% of the fimbrial end of the tube is removed and ligation is done. Unsuccessful mobilization of tubes was encountered in two patients, and these were done abdominally. The average hospital stay was 1.4 days including the day of operation. The mean follow-up period was 3.3 years and there was no failure.

Excision of Uterine Cornu

Littig[3], in his extensive review in 1912, concluded that the operation that is likely to give success is excision of all or part of the tube with deep, wedge-shaped excision of the uterine cornu including the pars uterina of the tube. Frequently the whole tube was removed. It has been pointed out[17] that the wedge resection of only the cornual portion of the tube has the technical advantages of: (1) simpler technique, (2) less exposure required, and (3) less interference with broad ligament ovarian blood supply. It is also equally effective. Some surgeons prefer to bury the proximal end of the remaining portion of the tube between the leaves of the broad ligament; but this is considered to be of doubtful value by others and it complicates the procedure. In Garb's review[1] the failure rate was 2.89%.

Other Methods

1. *Cooke Method.* After the divided tubes are ligated separately, the proximal limb is buried by going through the round ligament down between the leaves of the broad ligament. According to Overstreet[17] this method is widely used in the southern part of the United States.
2. *Aldridge Method.* This method[17] is desirable if temporary sterilization is foreseen. The fimbrial end is buried between the leaves of the broad ligament.
3. *Lyons Method.* Electrocoagulation is used to coagulate the tubes in three places 0.5 cm apart[18].

Pratt Operation

Regardless of the approach to the tubes, we think that, as a primary procedure, a thorough curettage of the uterus should be done. With the patient in the lithotomy position, we scrub the vagina with soap and water, paint it with thimerosal (Merthiolate), and then do a curettage (Figure 2). The endometrium is examined by frozen section. If there is no contraindication, we proceed with tubal ligation.

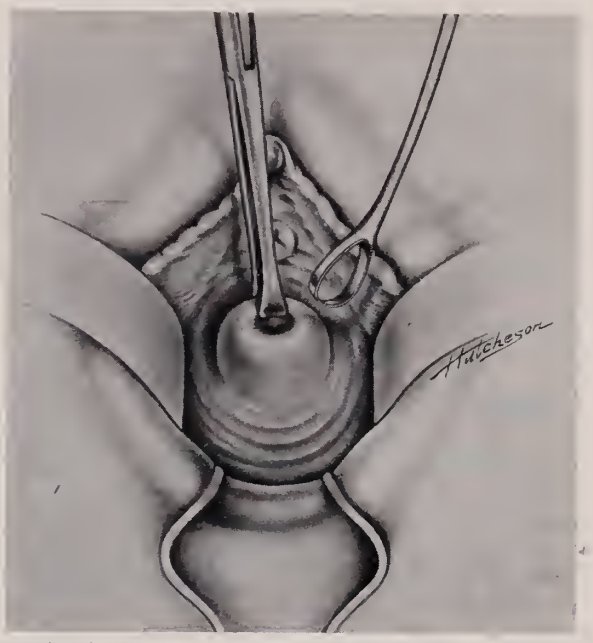


Fig. 2—Thorough, careful dilatation and curettage is always done before ligation procedure, to exclude pathology or pregnancy.



Fig. 3—Transvaginal salpingectomy and ligation are done through transverse incision behind cervix. Cervix is elevated to stretch posterior cul-de-sac. Frequently a small artery at either or both ends of incision must be ligated.

We prefer a transvaginal approach as being quicker and less traumatic to the patient, with simpler convalescence. The cul-de-sac is opened through a transverse incision immediately behind the cervix (Figure 3). A small artery at either end of the transverse incision frequently must be ligated. Two Deaver retractors are utilized through the cul-de-sac to expose the posterior uterine wall. The cervix can be elevated and pushed posteriorly with a tenaculum, abdominal pressure may be utilized, and the fundus is teased down until it presents at the posterior vaginal incision (Figure 4). The uterine end of one tube is grasped with a forceps and crushed (Figure 5-A). A second forceps is placed on the tube a full 3 cm away, and the remainder of the tube is inspected to rule out ectopic pregnancy. A 3 cm segment of tube is excised (Figure 5-B), the outer end is ligated with catgut, and the inner end, which is in the crushing forceps, is wedged from the wall of the uterus (Figure 5-C). The uterine wall is then closed with a mattress suture (Figure 5-D), the distal end of the tube is turned in on itself with an atraumatic stitch, and the tubal mesentery is closed, leaving the end of the distal tubal segment 2 cm or more from the uterus. A similar procedure is carried out for the opposite tube and both excised segments are sent to the pathology laboratory for unequivocal identification. All blood is sponged from the cul-de-sac, and the colpotomy incision is closed in two layers with a running catgut stitch in the peritoneum and a locked catgut stitch in the vaginal mucosa.

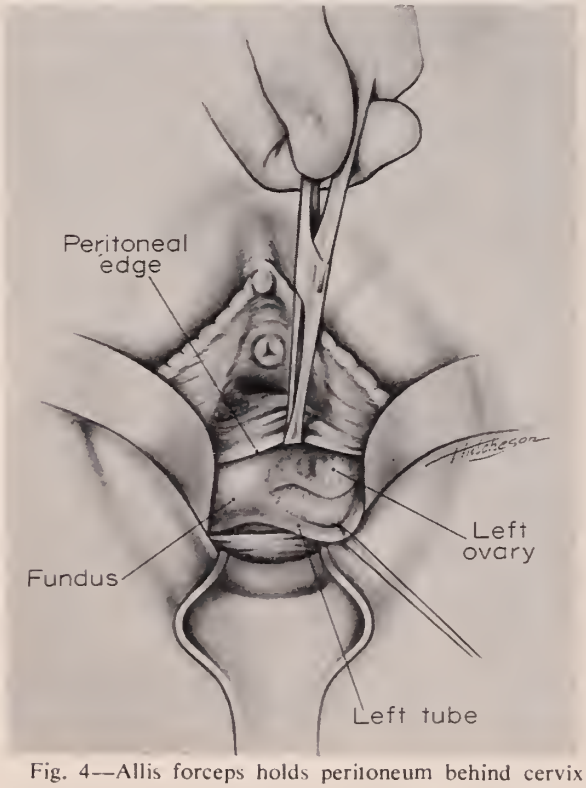


Fig. 4—Allis forceps holds peritoneum behind cervix and two Deaver retractors give adequate exposure to cul-de-sac. Uterine fundus is teased down until it presents at posterior vaginal incision. By moving fundus laterally, either tube and ovary can be exposed.

Laparoscopy

The introduction of the fiber glass bundle into optical equipment in 1964 made possible sterilization through laparoscopy. It is carried out with diathermy coagulation and dissection of about 2 cm of the tubal isthmus. Steptoe[19] emphasized thorough coagulation of the medial stump to prevent fistula formation. A question has been raised[20] as to whether or not resection is necessary, because this step sometimes causes inconvenient bleeding from the region of the stumps. Steptoe found postoperative patency in 10% of 30 women who had coagulation alone. In Steptoe's hands, bleeding is rare and can be controlled easily by the diathermy forceps. Liston and associates[20] had to perform laparotomy in six of their 760 patients to control such bleeding. Bleeding may occur from the inferior epigastric artery and require ligation[19]. The incidence of pregnancy was 0.2% in Steptoe's series, but nine pregnancies occured in Liston and associates' series (five women were pregnant at the time of operation). Two patients had had the round ligament resected instead of the tube. The major objection to the coagulation technique is that no tissue is available for pathologic confirmation that a portion of a tube has actually been blocked.

Complications

A specific operative complication of tubal sterilization is hematoma of the broad ligament. This is rarely reported. Other complications are those inherent in abdominal surgery in general—abdominal bleeding, infection, and cul-de-sac abscess.

The later complications to be mentioned are abnormal uterine bleeding, hydrosalpinx, and torsion of the tubes. Williams and associates[21] reported an incidence of 16.5% for significant abnormal bleeding after tubal ligation in contrast to 5.1% in women not undergoing such a procedure. White[22] reported heavier or more prolonged menses or irregularities in 20.6% of

patients; in Smith and Symmond's[16] series this problem was encountered in 8%.

The late psychologic aspects of sterilization have been given recent attention and reports differ significantly.

Because of difficulties in peritonealization in certain cases of cornual resection, adhesions may form and cause intestinal obstruction.

It was estimated by Paniagua and associates[23] that the mortality for tubal ligation may not exceed one per 10,000 cases when done for other than medical complications of pregnancy and is considerably less than that of childbearing itself.

Route of Approach for Tubal Sterilization

Tubal sterilization cannot be satisfactorily accomplished through the vagina in the immediate postpartum period, but this route can be used for nonpuerperal, interval tubal sterilization. This is frequently done by surgeons who do not wish to remove the uterus at the time of vaginal reparative surgery. It should be emphasized that the overall morbidity and failure rate in tubal sterilization are significantly higher when the vaginal route is used and are highest when it is done at the time of therapeutic abortion. The Madlener method has a 5.3% failure rate when done vaginally at abortion[24]. Cornual resection has a 2.89% failure rate when done through the abdominal wall but 36% when done vaginally at the time of abortion.

The failure rate for the Pomeroy technique is 0.3% when done postpartum abdominally and 5% when done vaginally as an interval procedure.

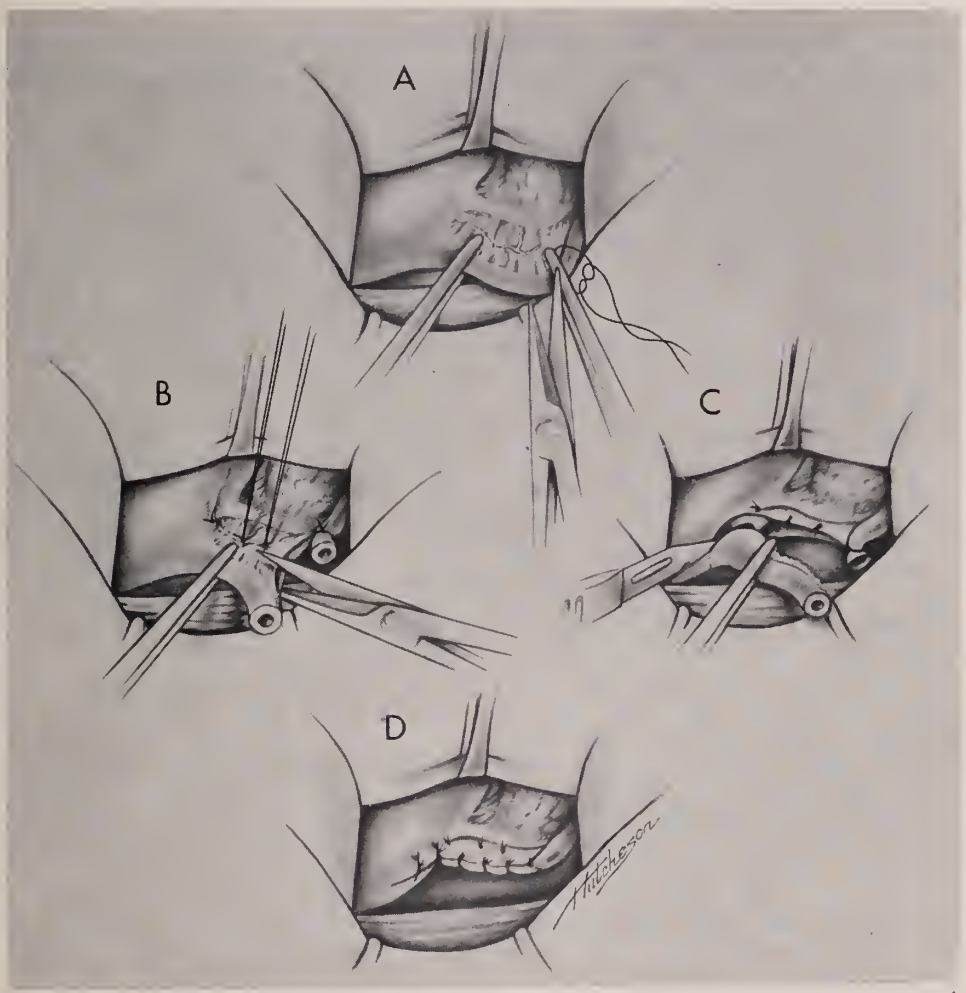


Fig. 5—(A) Tube is held at uterine end and about 3 cm laterally. Distal segment is divided and ligated. (B) Vessels in mesosalpinx must be ligated, as well as larger artery uniformly present in the uterine wall just below tube. (C) Uterine end of tube is wedged from wall of uterus. (D) Uterine wall is closed with mattress suture, distal segment is turned in on itself, and mesosalpinx is closed as well as possible.

For the Pomeroy method the morbidity has been found to be 3.3% when done vaginally[25] but 5% when done abdominally[26]. Among Smith and Symmond's[16] 161 patients having partial salpingectomy done vaginally there were three postoperative pelvic infections and two cases of postoperative bleeding, one from the culdotomy incision and one from a lacerated cervix, presumably from the tenaculum traction. The main difficulties were encountered in those patients who had adhesions from previous pelvic surgery or in recently pregnant women. They advised deferring operation for three to four months after parturition to allow complete uterine involution.

The Cooke and Irving methods are technically difficult if done via the vagina, and the Aldridge procedure cannot be accomplished vaginally.

Transuterine Cornual Coagulation

This operation has been revived several times since first recommended by Froriep in 1850. For some this operation has been tempting because of the speed and ease with which it can be performed. However, it never has become popular in the United States. Some work has been done with it in underdeveloped countries; Pasricha[27] reported doing this operation on 89 women in India. Fifty-three percent of those seen for follow-up examination had patent tubes demonstrable by hysterosalpingography. After a second attempt there were still 34% with patent tubes. Subsequent pregnancies were about 5%. Complications were numerous; salpingitis, severe bleeding, and peritonitis (one with bowel perforation) were reported.

Hysterectomy

Hysterectomy for sterilization alone may be accomplished in the course of vaginal reparative surgery or at the time of cesarean section. Frequently the uterus is removed in the course of reparative surgery without any mention of sterilization, and at present most surgeons consider it an integral part of the operation.

The utilization of cesarean hysterectomy has been a matter of dispute for a few decades. In 1921 Williams[6] described its use for preventing further pregnancies; he considered it the "most efficient method of relieving the existing situation and of effecting definitive sterility." Despite this report, the operation was not generally accepted as an elective sterilization method. It was considered by many as unnecessarily radical, as dangerous because of the greatly increased vascularity, and as difficult because of the uterine size.

In 1,278 cases of elective cesarean hysterectomy collected by Pletsch and Sandberg[28], there were only two maternal deaths (0.16%)—one due to pulmonary embolism and the other to hemorrhage from an unspecified site in a patient with leukemia. On the other hand, there were eight maternal deaths in 265 cases of indicated cesarean hysterectomy. Morbidity was about equal after cesarean hysterectomy and after cesarean section with tubal ligation, ranging from 5 to 30%. Various authors have compared the convalescence after cesarean hysterectomy to that after cesarean section and thought it was "easier," "smoother," "faster," or "shorter" after the former.

Operative complications are mainly excessive bleeding and perforation of the bladder. Up to 58% of the patients in Pletsch and Sandberg's series received blood transfusion, compared to up to 20% in the series of cesarean section and tubal ligation. The relatively high incidence of bladder laceration has been stressed, and in different series its incidence has been from 0.5 to 7.2%. The main postoperative complications are bleeding and hematoma formation, the latter ranging from 1.6% to 4.1% in different series.

Weed pointed out that as many as 14% of patients who had had cesarean section subsequently required a gynecologic surgical procedure, including hysterectomy[28]. Chesterman reported that hysterectomy is performed three times as often in women who have had cesarean section as in those who have been delivered vaginally[28].

In one of the most recent reports, Davis and McKeown[29] reviewed 751 cases at the Chicago Lying-In Hospital. There was no maternal mortality in their series and they stated that the incidence of complications was no greater after cesarean hysterectomy than after ordinary cesarean section when done by competent surgeons.

Summary

A brief history of gynecologic operations for sterilization is presented. The commonly utilized procedures are described and their advantages and disadvantages are stressed. A method of tubal ligation (that of one of us, J. H. P.) is presented. Pathologic identification of segments from both tubes is urged.

See References on page 293.

Ischemic Electrocardiographic Changes with Reversion

After Removal of Diseased Gallbladders

JOHN W. ANDERSON, M.D.*

It is often difficult to distinguish between the symptoms of coronary artery and biliary tract disease. Either of these entities may present with pain in the right, left or center chest or upper addomen. The pain in either may radiate to the right or left shoulder and arm, and acute episodes may have associated nausea or vomiting. Patients with either disease may be of similar body types and practice similar dietary habits, and both of these conditions are extremely common.

Of course, in some instances, the same patient may at the same time have both biliary tract disease and coronary artery disease, and even the possibility of etiological relationship between the two has been the subject of wide discussion for many years.[1,2]

The problem is made even more difficult by the fact that objective findings, namely electrocardiographic ST-T wave changes characteristic of myocardial ischemia and roentgenologic evidence of gallbladder disease, may coexist[3], in which case it is difficult to decide whether to attack the biliary tract problem surgically or to settle into management of the myocardial ischemia only. Some physicians are somewhat reluctant to advise elective removal of a diseased gallbladder in patients with electrocardiogram evidence of coronary artery disease, feeling that they may be poor surgical risks. This author has in recent years been influenced by the reports of other physicians[4] to advise removal of the gallbladder under such conditions, providing recent acute myocardial ischemia with suspected or proved infarction has been clearly disconfirmed, it being recognized that elective surgery during the first several months after myocardial infarction entails a high risk. It has been impressive to observe the frequency of good clinical results postoperatively, and even more important to observe the number of such cases that demonstrate a reversion of the ST-T waves to normal on postoperative electrocardiograms. The following three cases demonstrate this in varying aged patients:

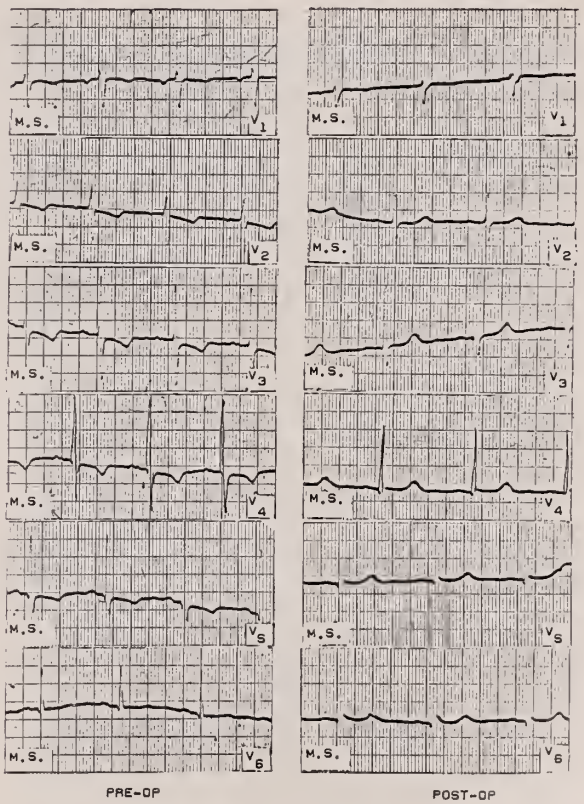


Fig. 1—V_{1-6} Pre-Op and Post-Op.

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This study was supported by the Blue Earth Medical Center, Blue Earth, Minnesota.
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Case Reports

Case One

A 77-year-old, widowed, white woman was first seen on February 21, 1968, because of episodes of tightness in her chest, at times radiating to both shoulders and arms, usually more severely to the right side. A physical examination was within normal limits. Extensive Xray and laboratory evaluation (to include serum enzymes) was within normal limits with the exception of the electrocardiogram (Figure 1) which demonstrated T wave changes characteristic of myocardial ischemia and the cholecystogram which demonstrated poor concentration of dye and one large gallstone (Figure 2). On the basis of the history and electrocardiogram findings it was thought that the patient might be in a so-called pre-infarction state, and she was hospitalized and treated accordingly. Her symptoms, however, worsened, to include vomiting, abdominal pain and an increase in the right shoulder pain. Because of this, her situation was re-evaluated and cholecystectomy advised. At operation the gallbladder was found to be thick walled from chronic inflammation and to contain one large stone. She withstood the surgery uneventfully. One year later, at which time she said she had been free of symptoms since her cholecystectomy, a repeat electrocardiogram (Figure 1) demonstrated reversion of the T wave changes that had been present on her preoperative electrocardiogram.

Case Two

A 59-year-old, married, white woman was first seen on December 9, 1968, because of episodes of pressure in her upper abdomen, usually after retiring for the night which at times actually delayed her being able to go to sleep. She also noted that her heart would pound during these episodes. A physical examination was within normal limits. Extensive Xray and laboratory evaluation (to include serum enzymes) was all within normal limits except for the electrocardiogram which demonstrated ST-T wave changes characteristic of myocardial ischemia (Fig. 3) and the cholecystogram which demonstrated numerous small gallstones (Fig. 4). The patient was placed on a treatment regime used for coronary insufficiency but without relief of her symptoms. She was advised to have a cholecystectomy which was performed six weeks after her first examination. At operation the gallbladder was found to be thick walled from chronic inflammation and to contain numerous small stones. Six months later, she had been free of symptoms since recovery from her cholecystectomy and a repeat electrocardiogram demonstrated reversion of the ST-T wave changes that had been noted on her preoperative electrocardiogram. Continued follow-up since then has revealed these normal conditions to persist.

Case Three

A 42-year-old, married, white woman was first seen on February 13, 1970, because of discomfort in her right abdomen. Numerous members of her family had been victims of cardiovascular disease. A physical ex-



Fig. 2—Xray (Case 1)—cholecystogram.

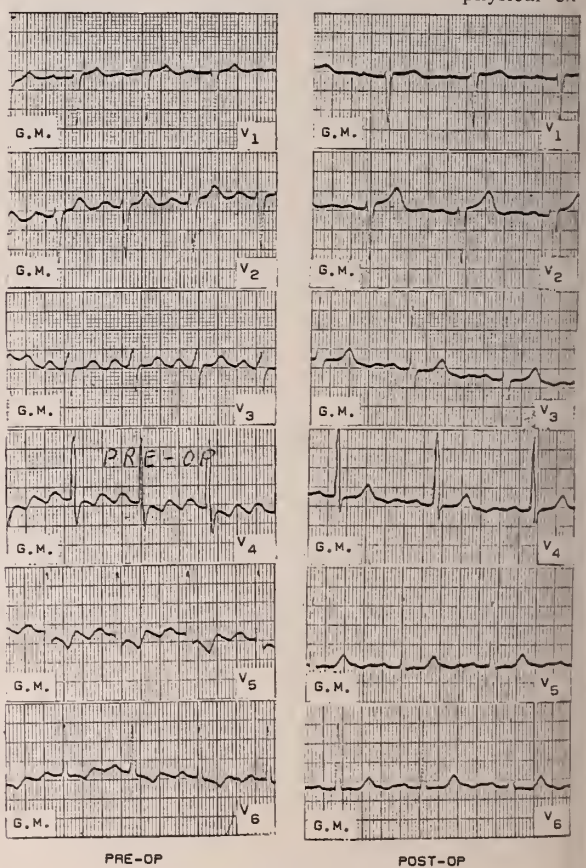


Fig. 3—V_{1-6} Pre-Op and Post-Op

amination was within normal limits. Extensive Xray and laboratory evaluation (to include serum enzymes) was within normal limits except for the electrocardiogram (Figure 5) which demonstrated T wave changes characteristic of myocardial ischemia and the cholecystogram which demonstrated a large gallstone (Figure 6). It was thought that the patient's signs and symptoms were related to her gallbladder disease so she was advised to have a cholecystectomy which was performed two weeks after her first examination. At operation the gallbladder was found to be thick walled from chronic inflammation and to contain one large stone. Five weeks later, she was free of her previous symptoms and a repeat electrocardiogram (Figure 5) demonstrated reversion of the ST-T wave changes that had been present preoperatively.

Comment

Electrocardiographic ST-T wave changes characteristic of myocardial ischemia from coronary artery disease have been found in patients with pancreatic disorders, hemorrhage in the upper gastrointestinal tract, metabolic disturbances, intracranial hemorrhage and infracardiac truncal vagotomy as well as biliary tract disease. T wave changes following subarachnoid hemorrhage have been attributed to vagal stimulation at the level

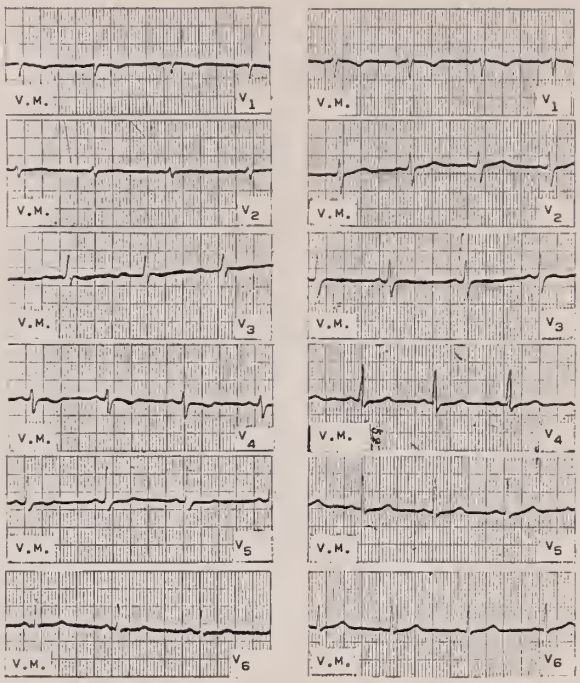


Fig. 5—V_{1-6} Pre-Op and Post-Op.

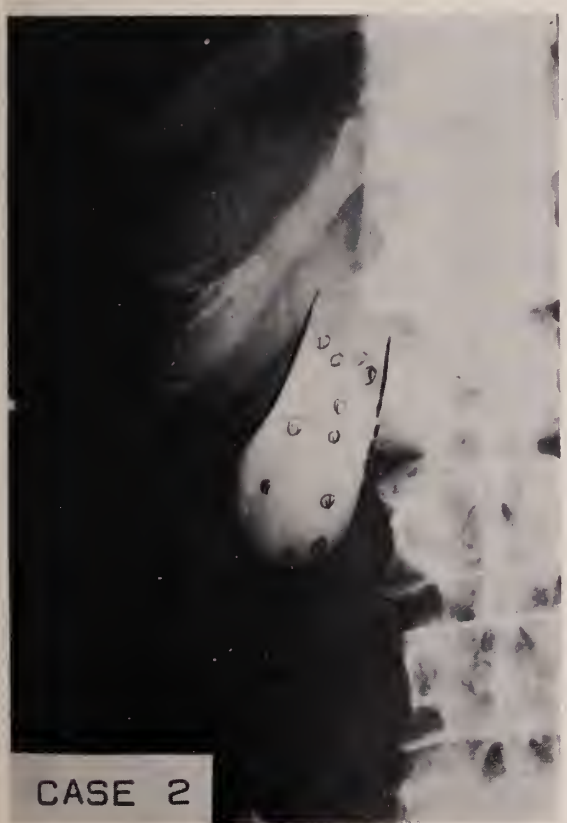


Fig. 4—Xray (Case 2)—cholecystogram



Fig. 6—Xray (Case 3)—cholecystogram

of the brain.[5] Animal experiments with paraffin cerebral embolism have shown abnormal T wave changes which were prevented by prior transection of the vagus.[6] In 1937 Manning et al.[7] reported the occurrence of myocardial damage in animals, with the presence of negative T waves, due to prolonged stimulation of the vagus nerve. This phenomenon was prevented by atropine and accentuated by physostigmine.[7] Frieden has postulated that the ST-T wave changes that may accompany biliary tract disease result from vagally mediated reflex coronary vasoconstriction via retrograde vagal conduction and central autonomic stimulation.[8]

It would appear from the work of the authors that biliary tract disease may in some patients exert a vagal, possibly deleterious, effect on the heart. Other authors have argued that an improved electrocardiogram after a cholecystectomy was merely an unrelated coincidence in the natural life history of coronary artery disease. However, it seems likely on the basis of both experimental and clinical observations that the relationship between gallbladder disease and myocardial ischemia is more than happenstance. Furthermore, in order to enhance the management of both conditions, it is probably advisable to perform Xray studies of the biliary tract in all patients with suspected or proved coronary artery disease and to perform electrocardiographic studies in all patients with suspected or proved biliary tract disease. Those found to have both diseases can be expected in some cases to show reversion of their electrocardiograms to normal after judicious and timely cholecystectomy, and, furthermore, to be some relieved of the dangers inherent in the complications of both biliary tract and coronary

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Cover Photograph

"Mexican Pilgrimage"

Dr. Robert L. Wilder, Minneapolis pediatrician, stated that the cover painting is his impression of the annual pilgrimage in February of the Mexicans of the central area of Mexico to the Shrine of the Virgin at San Juan de los Lagos, some miles east of Guadalajara.

Dr. Wilder's art training began after his retirement in 1957 with instructions obtained at the Minneapolis Art Institute, Minnetonka Center of Art and Education and the Instituto Allende Mexico.

He is a Fellow of the American Academy of Pediatrics, a former Clinical Associate Professor of Pediatrics of the University of Minnesota, and has memberships in the American Physicians' Art Association and the Society of Minnesota Sculptors.

Radiation and Leukemia Mortality

Proof or Spoof

DONALD E. BARBER, PH. D.*

It has been more than a year since statements concerning relationships between radiation exposure and leukemia began to appear in the news media in the Minneapolis-St. Paul area. These statements were made in conjunction with expressions of concern over construction of nuclear powered generating stations in Minnesota. The implication of the statements is that exposures to low levels of radioactivity released to the air and water will result in increased leukemia mortality in our population, particularly in young people.

Radiation doses of greater than 100 rads[1] are known to induce acute leukemia or chronic myelogenous leukemia, but *not* lymphocytic leukemia.[2,3] Findings of the Atomic Bomb Casualty Commission . . . "indicate that the leukemogenic effect of radiation was greater in children exposed to the bomb than in older persons. Among those under 10 years of age, the leukemia rate was 26 times higher if exposure was within 1500 meters of the hypocenter than when it was beyond that distance. In the next age group, 10 to 19 years of age at the time of exposure, the corresponding increase was 18 fold."[4]

There is no question that acute, high doses of radiation can induce leukemia, particularly in children. However, the effects of exposure to high doses accumulated over a long period of time and the effects of low doses remain open to question. For example, of 420 human cases involving radium ingestion there have been no proven cases of leukemia 30 to 50 years after radium was taken into the body in quantities as high as 40 uCi.[5] With each passing year it becomes increasingly difficult to support the premise that any amount of radiation exposure involves some risk (however small) of developing leukemia.

The Columbia River

Fadeley[6] in 1965 reported an increased mortality rate for cancer, including leukemia, among residents near the south bank of the Columbia River which receives radioactivity from a large national laboratory.

His suggestion of a possible causal relationship between radioactivity and his observed higher cancer mortality rate would be important if his observations could be confirmed. However, a reappraisal of his report by Bailar and Young[7] presented evidence to refute his suggestions. The solid lines in Figure 1 show the leukemia mortality on the south side of the Columbia River (Oregon) and on the north side of the river (Washington). The dashed line is the nationwide leukemia mortality for the white population. Fadeley considered only the leukemia mortality on the Oregon side of the river. As the figure shows, leukemia mortality is climbing on that side of the river, but there appears to be a trend toward leveling off similar to that in the U.S. white population in the early fifties.

If one wishes to argue about the differences between the U.S. and the river county curves in this figure, it is interesting to note that the mortality

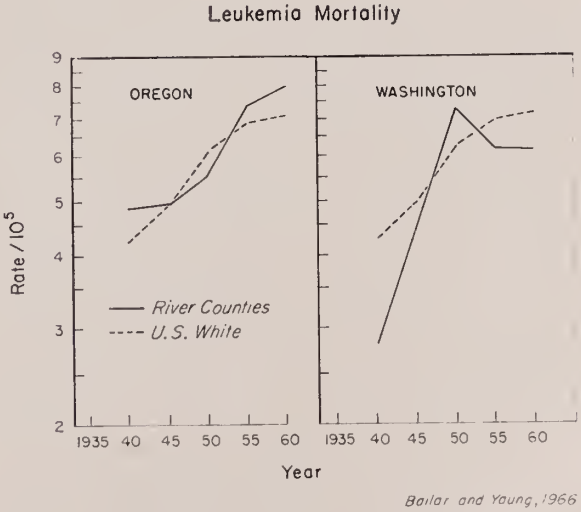


Fig. 1—Leukemia mortality on the Columbia River, 1940-60.

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rate, even on the Oregon side of the river, prior to major operations at the national laboratory, about 1945, was higher than in the U.S. white population. After the laboratory went into operation the leukemia mortality along the Oregon side of the river stayed below that for the mortality in the U.S. white population until the early 50s. But the differences between the two curves in the figure are not significant because wide variations are found from year to year in leukemia mortality data from whatever source. On the basis of the Oregon data alone, it is difficult to see how one can conclude that radioactivity from the laboratory influenced the leukemia mortality on the south side of the Columbia River.

Leukemia mortality in the counties on the north side of the Columbia River presents an entirely different picture but one which makes it even more difficult to justify any causal relationship between the radioactivity in the Columbia River and the leukemia mortality in residents downriver from the source of that activity. If one insists that the differences in the figure are significant and related to radioactivity, one is led to the conclusion that the radioactivity from the laboratory has been of benefit to residents on the Washington side of the river.

Nationwide Leukemia Mortality

Figure 2 shows the nationwide leukemia mortality rate for white males for a number of age groups.[8] Except for the age groups under one year and over 75, the curves for all age groups are similar in shape, but mortality rates in any five year period since 1928 are highest for age groups one to four and 45 to 54 (the latter group not shown on this figure) until about 1953 when the rate in the age group over 75 overtook the rates in all other groups. It is interesting to note from this figure that leveling off of leukemia mortality and declining mortality in the younger age groups, the age groups of most concern, one to four and five to 14, occur during the very years when radioactivity from fallout was being contributed to our environment at the greatest rate.

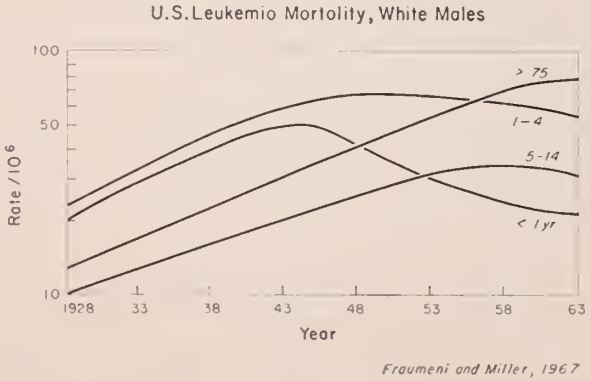
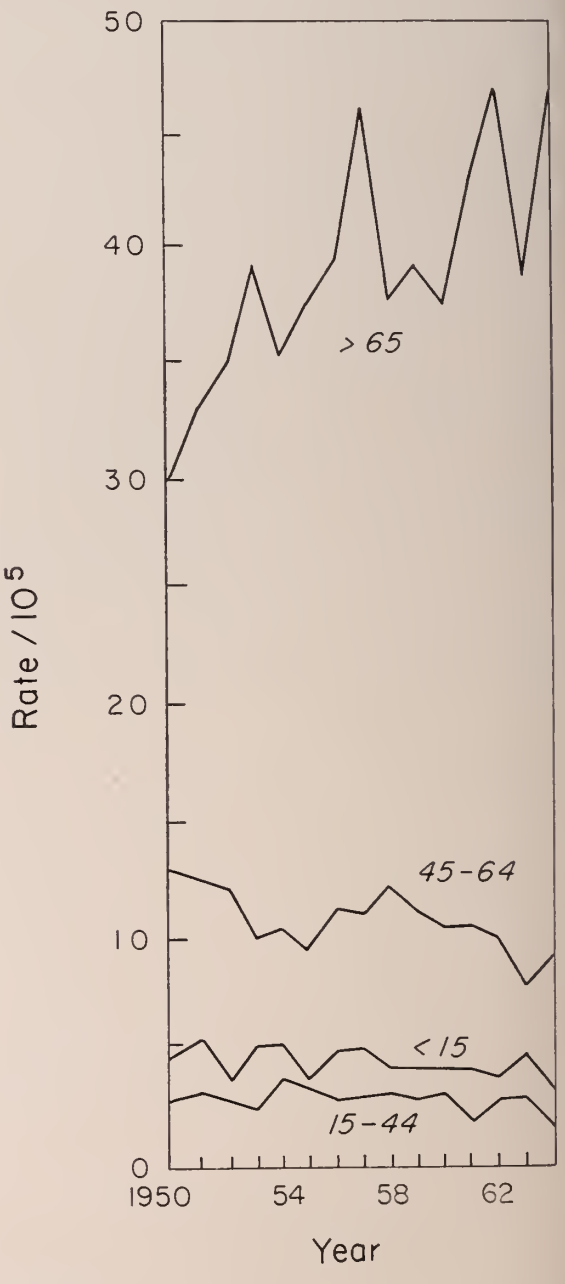


Fig. 2—Nationwide leukemia mortality.

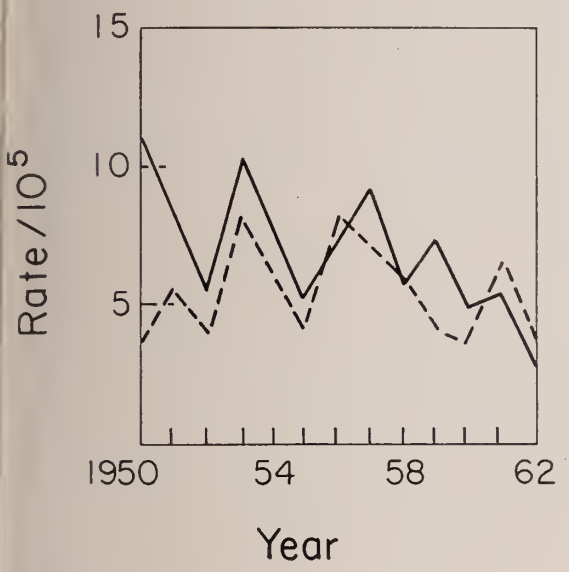


From McCullough, et. al., 1967.

Fig. 3—Minnesota leukemia mortality.

Minnesota Leukemia Mortality

From 1929 to 1951 Minnesota has had either the highest or the second highest leukemia mortality of any state in the country. Minnesota was surpassed by Vermont in the years 1949 to 1951 and by the District of Columbia in the years 1939 to 1941.[9] Figure 3 shows the Minnesota leukemia mortality rate for the years 1950 to 1964 for four different age groups. The fluctuations are huge for the age groups over 65. For ages zero to four, we see in Figure 4 a declining trend in leukemia mortality among males; but no trend is apparent in females.



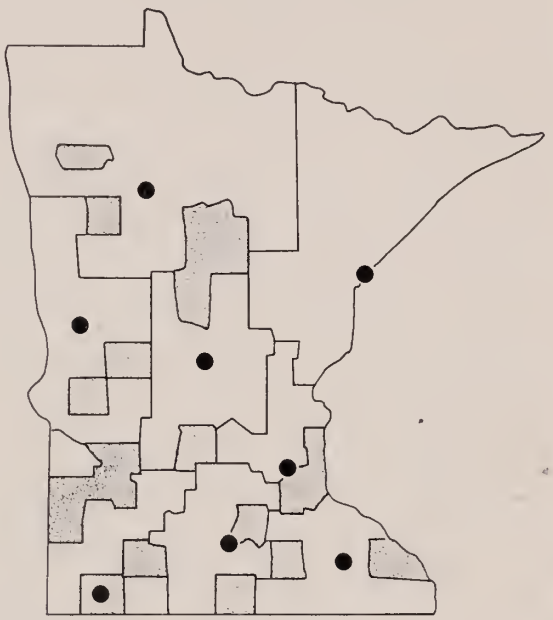
From McCullough, et. al., 1967.

Fig. 4—Minnesota leukemia mortality, ages zero to four.

Highest Mortality with Lowest Fallout Exposure

In some counties in Minnesota the average, annual, age-adjusted leukemia mortality rate for the years 1950 to 1964 varied significantly from the average state rate for that same period.[10] The highest rate occurred in Wabasha County in southeastern Minnesota where exposure to fallout is low by comparison with northern Minnesota.[11] Concentrations of strontium-90 in milk in northern Minnesota have been one-and-a-half to two times those in southern Minnesota since 1962.[11] A similar picture occurs for cesium-137 concentrations in milk.[12]

Figure 5 shows the state health districts, milk sampling stations and counties (gray areas) in the state with highest age-adjusted leukemia mortality for the years 1950 to 1964.[10,12] The important feature of this figure is the relatively higher leukemia mortality in the southern part of the state where radioactive contamination of milk from fallout is lower than in the northern part of the state.[7,10] Duluth, however, did not have higher rates compared with St. Louis County.[10]



From McCullough, et. al., 1967 and Radiological Health Data and Reports, 1968.

Fig. 5—Minnesota health districts, milk sample stations (●) and counties (gray areas) with highest age-adjusted leukemia mortality, 1950-64.

Radioactivity of Drinking Water

Radioactivity entering the body commonly does so by way of food, except where unusually high concentrations occur in water. Typical concentrations of Radium-226 in *city drinking water* range from 0.01 to 0.14 pCi/1. But concentrations in *rural drinking water* range from 0.03 to 2.3 pCi/1.[13] Radium-226 concentrations in rural drinking water, therefore, are from three to 20 times concentrations for urban supplies. Like strontium-90, radium is a bone seeker and bone is a critical tissue from the viewpoint of leukemia production. If the quality factor for alpha rays from radium is taken to be 10, then Radium-226 contributes a substantial fraction, from seven to 30 per cent, of the total background dose to bone. So, if either background radiation or fallout is responsible for increasing leukemia mortal-

ity in the population and if population density is a factor contributing to the correct interpretation of leukemia mortality data, it is difficult to reconcile the distribution of the leukemia mortality statistics in Minnesota with radiation exposure.

Discussion

The nationwide picture of leukemia shows that the mortality rate in all age groups except for those over 75 has leveled off and is decreasing. We know that dose rates vary from time to time from fallout and other sources of radioactivity and radiation, but the total or integral dose to which an individual is exposed can only grow larger with the passage of time. If the assumption is true that there is no threshold for radiation induced leukemia, then the nationwide mortality rate data are inconsistent with that hypothesis. Apparently the years of highest radiation exposure, 1945-63, during which the greatest amount of radioactive material was ingested have not influenced the trends observed in the nationwide leukemia mortality statistics.

Dose rates, and therefore doses, in the years 1958-1959 and 1962-1963 from fallout would have been highest for the fetus in the first trimester and infants. Consequently, leukemia mortality would be expected to increase five to ten years later or about 1963 to 1969 and 1967 to 1973. However, the mortality statistics for these periods do not reflect evidence of a special sensitivity of the young to radioactivity from fallout.

A legitimate question is: even on the assumption that there is no threshold for radiation induced leukemia, would one expect to see manifestations of this fact in our leukemia mortality statistics? According to Hempelmann the risk of developing leukemia is about one case per million people per rad absorbed per year.[14] If this risk statement is true, then over a period of 20 years we would anticipate an increase in the leukemia rate produced by background radiation alone of at least two cases per million. We would certainly not expect a decline in the mortality rate unless improvements in radiation exposure had been made and in fact radiation exposure had contributed to the increase in leukemia mortality over the years. Fraumeni and Miller have suggested that improvements in medical x-ray exposure may explain the downturn in leukemia mortality rates in the United States during the late 50's and early 60's.[8] However, if the assumption is correct that the risk of inducing leukemia with radiation is about one case per million per rad per year, then the downturn rates observed by Miller and Fraumeni are much too large.

It is an interesting coincidence that nationwide leukemia mortality rates began to level off during the years 1943 to 1948. Fallout has been with us since that period. The years 1945 to 1949 were years in which a tremendous surge in the use of antibiotics occurred. DDT was first used about 1944 and was used extensively until the early fifties. Thereafter new insecticides and artificial fertilizers were widely used. All of these activities correlate with observed trends shown in the nationwide leukemia mortality data. The possibility that these agents influenced leukemia mortality seems as amenable to proof as the suggestion that reduction in medical exposure is responsible for a downturn rate in the leukemia mortality data. Perhaps the change in leukemia mortality has occurred in spite of radiation rather than because of it.

Conclusions

I have pointed out, perhaps facetiously, a number of observations which are inconsistent with an hypothesis that low levels of radiation exposure increase the leukemia mortality rate. These observations are:

1. The general pattern of nationwide leukemia mortality rates during the years 1923 to 1963 has changed.
2. The relative concentrations of radium in drinking water supplies available to urban and rural populations, suggest an inverse relation between exposure and leukemia mortality.
3. Leukemia appears to be more prevalent in southern Minnesota than in northern Minnesota, but the exposure to fallout activity through the milk-food chain appears to be lower in the south than in the north.
4. There is no evidence that persons living downstream from the national laboratory on the Columbia River had an excess risk of death from leukemia by virtue of their location, presumably from the run off from a large national laboratory.
5. If exposure to environmental factors, including radiation, is responsible for leukemia, exposure has either stabilized or decreased during the period 1940-1963.

Human data prove that doses of 100 rads or more received in a short period of time increase the risk of developing leukemia. On the other hand, attempts to establish a causal relationship between leukemia mortality and lesser doses, particularly those accumulated over a long period of time, appear to involve more spoof than proof. Miller expresses my feeling perhaps better than I could express it myself when he writes, "The total number of delayed organic effects of atomic irradiation among Japanese children has been small. The most prevalent late effect, difficult to document, is the fear of late effects, a most unfortunate circumstance in view of the small risk indicated by the results to date."[4]

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Everybody's family doctor was remarkably clever, and was understood to have immeasurable skill in the management and training of the most skittish or vicious diseases. The evidence of his cleverness was of the higher intuitive order, lying in his lady 'patients' immovable conviction, and was unassailable by any objection except that their intuitions were opposed by others equally strong; each lady who saw medical truth in "the strengthening treatment": regarding "the lowering system" as medical perdition. For the heroic times of copious bleeding and blistering had not yet departed, still less the times of thorough-going theory, when disease in general was called by some bad name, and treated accordingly without shilly-shally—as if, for example, it were to be called insurrection, which must not be fired on with blank-cartridge, but have its blood drawn at once. The strentheners and the lowerers were all "clever" men in somebody's opinion, which is really as much as can be said for any living talents.*

*George Eliot: Middlemarch, Book 11 Chapter 15. 1871-1872. (describing the family physician of 1830.)

Primary Pulmonary Fibroma

JOHN J. SAUK, JR., D.D.S., M.S.D.*, MARIO PLIEGO, M.D.† AND
W. ROBERT ANDERSON, M.D.‡

THE PRIMARY PULMONARY fibroma is among the rare group of primary mesenchymal tumors of the lung. The entity, however, must be distinguished from its sister mesenchymal neoplasms, the leiomyoma, the neurofibroma, and the fibrous mesothelioma.

D'Aste,[1] in 1955, documented only 15 such lesions, classified as pulmonary fibroma from 1926 to 1952, and gives Sauerbruch credit for the first reported case in modern medical literature. Other cases documented since D'Aste's paper[2-6] have further alluded to the entity, and have defined it more completely with the use of histochemical stains, and the identification of possible pleural origin, separating the fibrous mesothelioma as a separate and discrete lesion.

Case Report

The patient, an 84-year-old Caucasian male, first presented in 1964 with a respiratory distress syndrome. Radiologic examination revealed a large mass in the right lower lobe of the lung. The patient refused any surgical or therapeutic intervention, but was followed regularly at Hennepin County General Hospital.

Radiologic Reports

The first radiograph taken at Hennepin County General Hospital March 16, 1964, an anteroposterior view of the chest, revealed a large multilobulated, smoothly outlined, dense, homogeneous shadow lying in the lower half of the right lower lobe. The mass was within the lung parenchyma, and some portion of it appeared to be in close proximity to the right pleural space. The lesion at that time measured 12 x 7 cm, and presented several eccentric calcifications within it and other small calcifications situated at the upper lobes, probably due to calcified granuloma. The heart was enlarged, left ventricular predominance. The aorta was calcified. There was a fracture deformity of the fifth right rib.

Subsequent radiographs done in 1965, 1966, and 1967, revealed no great change in the size and shape of the tumor. The last radiographs taken were in June, 1969, in which most of the tumor was obliterated by fluid, the patient being in congestive heart failure with enlargement of the heart, pulmonary vascular congestion and bilateral



Fig. 1—Anteroposterior and lateral radiographs taken in 1964 showing a radiopague mass in the lower right lobe of the right lung.

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‡Associate Pathologist, Hennepin County General Hospital.

pleural effusion.

In June of 1969 the patient was admitted with severe respiratory distress and a clinical diagnosis of bronchial pneumonia and congestive heart failure. His clinical course became terminal only days after admission. The body was presented for autopsy the day of death.

Autopsy Report

The autopsy revealed a well developed, well nourished 84-year-old Caucasian weighing approximately 150 pounds and showing no gross physical external abnormalities.

The heart weighed 700 grams. The right ventricle was 5 mm thick; the intraventricular septum, 7 mm thick; and the left verticle 20 mm thick. All valves were normal; the coronary ostia and the coronary arteries were patent. Organ diagnosis was that of cardiomegaly secondary to hypertension and cor pulmonale.

The lungs weighed 2250 grams combined. The pleural surfaces were diffusely anthracotically pigmented. Crepitus was markedly decreased. The parenchyma was severely congested with voluminous amounts of fluid; small nodular consolidations (bronchial pneumonia) were located throughout the parenchyma.

A large mass, 10 cm x 10 cm x 5 cm, was present in the right lower lobe of the right lung but did not involve either the viseral or the parietal pleura. On cut section it was yellow-gray in color and showed central necrosis. The trachea and main stem bronchi were not involved but showed a mucopurulent exudate.

The remainder of the gross autopsy was noncontributive.

Microscopic Examination

Microscopic examination of the lung revealed a tumerous mass, showing central necrosis. The viable cells showed a spindled cell pattern. The nuclei of the mass were slightly hyperchromatic but regular in size. A high degree of collagen formation was present intracellularly. Interlacing bundles typify the general tumor pattern. Mitoses were rare within the tumor and the mass appeared to be microscopically free from the pleura and bronchi.

Diagnosis

Intraparenchymal Primary Pulmonary Fibroma. (Low Grade Fibrosarcoma?)

Discussion

The problem of delineation of pulmonary fibromas from their sister neoplasms has resulted in confusion, especially with regard to their incidence, as many reports refer to the origin of the entity lying within the thoracic wall, the mediastinum, or the visceral pleura.[7-13] It is the belief of these authors and others[2-4] that the clinicopathologic term for those lesions, arising in the



Fig. 2—Anteroposterior and lateral radiographs showing the unchanged course of the lesion after three years.

interlobar fissures, parietal and visceral pleura, should be fibrous mesotheliomas.

Other diagnoses that often tend to confuse the label of pulmonary fibroma are the low-grade pulmonary fibrosarcoma, and various inflammatory fibroses discovered within the lung. The criteria to delineate low-grade fibrosarcoma have been: cellularity of the lesion, the amount of desmoplasia present, and the duration of the lesion. Mitoses in both instances have been considered rare, and cellular atypia is not present in well differentiated cases of the former. The duration of the lesions in both cases is relatively the same, being long, and metastasis does not occur in either. Therefore, lesions which have been highly cellular and have had little to no desmoplasia have been considered to be fibrosarcomas. It must be noted that even these criteria vary from microscopist to microscopist, and in some cases the final diagnosis is still a question of academic preference.

Inflammatory fibroses also present a problem in diagnosis, especially when biopsy is the method.

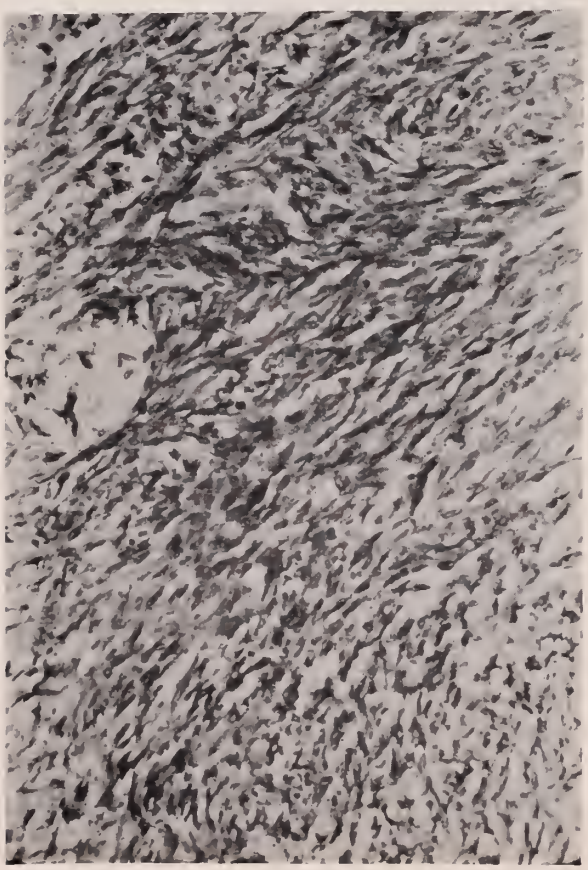


Fig. 3—High dry view (450X) showing the regular cellularity, interlacing pattern of cells, and desmoplasia.

However, with an inflammatory history, endothelial proliferation, and the presence or absence of inflammatory cells a reasonable diagnosis of neoplasia versus inflammation can usually be made. In spite of such guidelines, reports of pulmonary fibromas referred to as "hamartoblastomas" have in the same text described these entities both as neoplastic and "granuloma-like."[13]

Classically two types of pulmonary fibromas have been described, those occurring in the endobronchial tree, or an extension thereof, and those located completely within the parenchyma of the lung.[1,3,4] Likewise fibrosarcomas of the lung are also divided into those of the parenchyma and those of the endobronchial tree.

Fibromas of the endobronchial tree usually lend themselves to bronchoscopic examination and are visualized as pinkish-gray polypoid lesions. Those within the parenchyma proper are first observed on radiologic examination of the chest and present as solitary, circumscribed pulmonary densities. Differential diagnosis in both cases is usually quite broad because of the rarity of the lesion; an unexpected diagnosis is elicited by thoracotomy or by autopsy.

Review of the literature and examination of the clinical data reveal that the average age distribution for pulmonary fibromas is between 24 and 84 years of age, with an average 55 years.

The sex ratio is 65% males and 35% females. In all cases the racial distribution was limited to the Caucasian race.

The duration of symptoms have ranged from a period of one month to five years, with an average of two years. Presenting symptoms have been shortness of breath and, when the lesion has been exceedingly large, cor pulmonale with associated congestive heart failure.

The location of lesions has been evenly distributed both within the parenchyma and within the endobronchial tree. The lobar location has been 40 percent in the right lower lobe and 40 percent in the left lower lobe, with the rest located in the remaining lobes.

Treatment in all cases has been best achieved by surgical removal, usually local excision. The prognosis has been excellent unless a large amount of lung parenchyma has been previously destroyed by infectious or neoplastic processes.

Summary

In summary a rare mesenchymal neoplasm has been discussed with regard to sex incidence, location, classification, and therapy. This rare pulmonary neoplasm, pulmonary fibroma, has been documented in an 84-year-old male Caucasian and has served as a model for discussion and an addition to the archives of the world literature.

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It's the Law

Honest Misdiagnosis Held Not To Be Malpractice

A five-year-old child had vomiting and stomach-ache with pain in the lower right side of her abdomen, and a temperature of 101. The white blood cell count was 5,000. The child was examined by a physician who found red tonsils and made the diagnosis of tonsillitis. He gave the parents medication for the child and sent her home.

On the seventh day of her illness, the child was still complaining of stomach pain. She was admitted to the hospital and the white blood cell count was 18,000. Xrays were made, and surgery was performed. This disclosed a ruptured appendix with peritonitis. There was a complicated hospital course with a bowel obstruction, much wound drainage and a penicillin reaction.

The child's father sued the physician for malpractice. The courts held that a physician does not insure correctness of diagnosis. Evidence had been presented that the patient received a thorough examination conducted with diligence and skill. The court held that the physician was not negligent, hence, no malpractice and the suit was dismissed.

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Minneapolis, Minnesota

Sinkey v. Surgical Associates, 186 N.W. 2d. 658 (Iowa Sup. Ct., May 5, 1971) The Citation 23:9, August 15, 1971.

Prostatic Urethral Calculus

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CALCULI PRESENTING in the urethra are not uncommon, but a large calculus in the prostatic urethra without a previous prostatectomy is rare and is reported below.

Case Report

A 39-year-old white male was born with a lumbar myelomeningocele which was repaired in the newborn period. The patient had had no follow-up since and had been incontinent of urine and feces for which he has worn diapers all his life. He lived on a farm with his parents and had no education which resulted in poor speech and illiteracy. He also has bilateral clubbed feet but was fully ambulatory.

Examination

He was admitted to our hospital on December 18, 1968, acutely ill with retention of urine, urinary tract infection and renal failure. The urine cultured Proteus mirabilis over 100,000 cols/ml. Other laboratory results were Hb 17.4 gm%, Na 119, Cl 97, K 8mEq/1 and blood urea 108 mg%. A rectal examination revealed an enlarged and stony hard prostate. A urethral catheter could not be passed due to obstruction in the prostatic region. A KUB x-ray revealed two stones in the pelvis (Figure 1A), and a retrograde urethrogram demonstrated the larger stone to be in the prostatic urethra. (Figure 1B) After correction of the hyperkalemia and dehydration a suprapubic cystostomy was performed on December 19, 1968, with removal of the 6 cms diameter stone (117 gms) (Figure 2) from the prostatic urethra and a smaller stone (17 gms) from the bladder.

Appropriate intravenous fluids and antibiotics were given postoperatively, and his condition improved although the postoperative course was complicated by a gastrointestinal hemorrhage requiring blood transfusion. The blood urea fell to 34 mgm%, and a creatinine clearance was 34 liters/day/1.73 $M.^2$ An infusion excretory urogram (Figure 3A) and retrograde pyelograms revealed bilateral hydronephrosis and hydroureters with reduced renal parenchyma.

A cystogram (Figure 3B) and cystoscopy revealed a neurogenic bladder which allowed urinary incontinence when the suprapubic tube was clamped.

On January 28, 1969, a urinary diversion was performed consisting of an isolated segment of transverse colon with the open ends anastomosed to the pelves of



Fig. 1A—KUB x-ray examination of the pelvis revealing two stones.



Fig. 1B—Retrograde urethrogram demonstrates larger stone to be in prostatic urethra.

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he kidneys and the mid-portion brought to the skin as an ostomy. Urine culture from each kidney at operation revealed Pseudomonas over 100,000 cols/ml.

Postoperative Course

The postoperative course demonstrated some improvement of renal function, and the patient was discharged on February 25, 1969, with a blood urea of 35 mgm% and a creatinine clearance of 47 liters/day/1.73 M^2, and serum Na 140, K 4.1, CO_2 21, Cl 104, Meq/L. The stool cultured Pseudomonas over 100,000 cols/ml.

Discussion

A prostatic urethral calculus arises either from within the prostate gland (endogenous), within pockets or diverticula in the posterior urethra or reached the urethra from the kidney, ureter or bladder (exogenous).[1]

In our patient the calculus was thought to be exogenous and arose in the neurogenic bladder associated with his myelomeningocele. The calculus migrated to the posterior urethra where it enlarged to greatly expand the prostatic urethra and compress the prostate tissue.

Giant prostatic urethral calculi are rare, and 16 cases have been described[1-12]; the actual weight (45, 58, 80, 99, 327, 390, 780 gms.) and the size (two to 10 cms. longest dimension) are recorded in 10 of these cases. The calculus in our patient weighed 117 gms. and measured 6x5x5 cms which allows it to be designated as a giant prostatic urethral calculus.

A giant prostatic urethral calculus would, presumably, completely obstruct the flow of urine through the urethra. Grooves were present on the posterior aspect of the calculus, corresponding to the urethral crest and verumontanum, which would possibly allow the passage of some urine past the calculus. Similar grooves have been recorded in two cases of giant prostatic urethral calculus.[1,11]

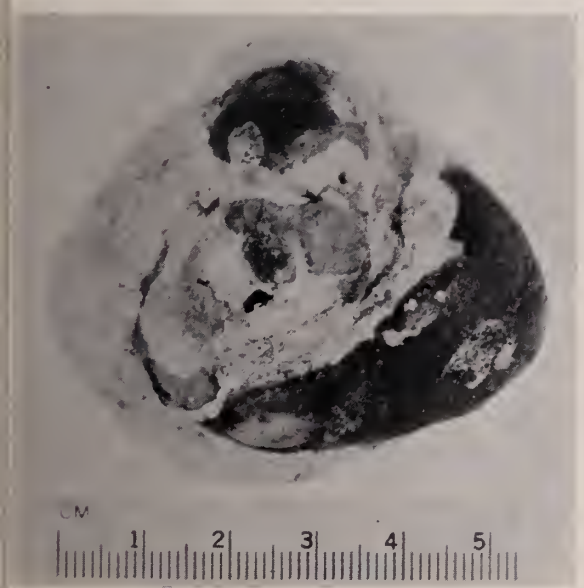


Fig. 2—Calculus removed from the prostatic urethra; posterior aspect shown with grooves visible.

Summary

A prostatic urethral calculus, weighing 117



Fig. 3A—An infusion excretory urogram revealing bilateral hydronephrosis.



Fig. 3B—A cystogram via the suprapubic tube demonstrated a neurogenic bladder with diverticula and left ureteral reflux with hydronephrosis and hydroureter.

gms and measuring 6x5x5 cms was found in a 39-year-old male with myelomeningocele who presented with retention of urine, urinary infection and renal failure.

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Letter to the Editor

Dear Editor:

I was pleased to find in the February, 1972, MINNESOTA MEDICINE* a reference to a charming fantasy. Dr. Charles Jarvis introduces his article *"Osmolality"* by saying, "Some years ago H. L. Gold wrote a little story about a man who got into trouble with the elves of a certain lake. As punishment the elves decreed that water would actively stay away from him. Since he was at the lake primarily to fish, but wanted also to bathe and drink, the results of the decree proved frustrating to the hero and amusing to the reader."

The story is "Trouble With Water" by L. E. Gold (Dr. Jarvis' memory misled him slightly—H. L. Gold is a younger writer). It appeared in the late John W. Campbell's magazine, *Unknown Worlds*, and was reprinted in the anthology *From Unknown Worlds* (New York, 1948).

As the slogan of the Los Angeles Science Fantasy Society puts it, "Death does not release you" (from membership). Dr. Jarvis has long since ceased to be active as a fan of fantasy-literature, but he was once well known in the field and clearly remains fond of it. Redd Boggs, in his article on the growth of Minnesota science fiction fandom ("Giants in Those Days," Part I, which I printed in *NeoLithic* 19, October 1961) described the young Charles W. Jarvis, "who had become one of the most prolific and talked-about letterhacks in "Brass Tacks" [the letter column of *Astounding Science Fiction, Unknown World's* older and more successful sister magazine]. Jarvis dabbled briefly in fandom—he mentioned receiving news about Grey Lensman from the fan magazines in a letter published October 1939—and in the thirties attended a number of meetings of the Minneapolis Fantasy Society. One of the few old-time fans residing in this area, Jarvis told me in March 1961 that he gave up reading Science Fiction years ago, but he mentioned some of the old sf classics with great nostalgia.

*Page 173.

Sincerely,
Ruth Berman

Laboratory Letter

Biocycling

"1st, have something to say; 2nd, say it; 3rd, stop when you've said it; 4th, give it an accurate title."—John Shaw Billings, M.D., 1828-1913, Prescription for Writing a Medical Paper.

Months ago in this journal* I wrote a paper "Parable of a Punctured Pathologist" saying the physiological variations of a prodigal pathologist's SMA-12/60 results far outstripped the analytical variation of the SMA-12/60 machine.

I laid it on the table:

TABLE 1

Quality Control Data on Daily Serum Samples of Pathologist After Various Physiological Events

	Physiological Variation	Analytical Variation	Ratio of Physiological to Analytical Variation
Calcium	0.15	0.1	1.5 times
Phosphorus	0.4	0.1	4.0 times
Glucose	18	2	9.0 times
BUN	3.0	0.4	7.5 times
Uric Acid	1.1	0.2	5.5 times
Cholesterol	16	6	2.7 times
T. Protein	0.2	0.1	2.0 times
Albumin	0.25	0.1	2.5 times
T. Bilirubin	0.6	0.04	15.0 times
Alk. P'tase	2.5	1.1	2.3 times
LDH	4.5	5.5	0.8 times
SGOT	6.0	2.7	2.2 times

Now some of you are saying the results are invalid because the pathologist didn't behave normally: too much food, too much drink, too much fasting. Just too much of the wrong things at the wrong time in the wrong amounts.

He was, in short, unfit for such an experiment.

Well-maybe he was and maybe he was not.

I discussed the matter with the fittest person I could find, a biochemist. He's fit because he bicycles eight and one-half miles to work and eight and one-half miles home again five days a week. On weekends, he really stretches out, sometimes pedalling 100 miles. He keeps fit, he says, partly because of diabetes, detected during childhood and requiring insulin. Anyway, he said he was going on a 211 mile bicycle marathon (107 miles on Saturday and 104 miles on Sunday). He would be at his fittest then and would be glad to confound the critics by repeating the experiment on himself. OK, I said, but no alcohol, no high protein meals, no non-fasting specimens, no hanky panky. All specimens to be drawn fasting at 8:30 A.M. after the eight and one-half mile ride to work. Everything had to be fit as a fiddle.

Here are the results for the skeptics of physiological variation.

TABLE 2

Analytical Variation of SMA-12/60 Results on Five Aliquots of One Serum Sample of Bicycling Biochemist

	Mean	Standard Deviation	Analytical Variation
Calcium	9.9	0.12	1.3%
Phosphorus	3.2	0.05	1.6%
Glucose	83.0	1.0	1.2%
BUN	17.2	0.4	2.3%
Uric Acid	3.1	0.17	5.5%
Cholesterol	266	10	3.7%
T. Protein	8.0	0.17	2.2%
Albumin	4.3	0.17	4.0%
T. Bilirubin	1.2	0.05	4.2%
Alk. P'tase	73	3.3	4.2%
LDH	172	8.8	4.5%
SGOT	56	2.8	5.0%

*December, 1971 issue, page 1035.

TABLE 3
Daily Changes of SMA-12/60 Chemistries of Bicycling Biochemist Before and After 211 Mile Bicycle Trip: Samples Drawn at 8:30 A.M. in Fasting State After 8½ Mile Ride to Work

	Pre-Trip	Immediately After 211 Mi. Bike Ride	One Day After	Two Days After	Three Days After	Four Days After	Five Days After	Eight Days After	Eleven Days After	Twenty Days After
Calcium	9.6	10.4	9.3	9.4	9.0	9.7	10.2	10.0	10.0	9.9
Phosphorus	3.4	5.2	3.3	2.9	2.9	3.3	3.7	4.5	4.1	3.2
Glucose	155	55	67	62	55	95	245	100	77	83
BUN	21	32	25	17	22	22	27	24	25	17
Uric Acid	2.8	4.8	2.7	2.8	2.4	2.1	1.9	3.2	3.4	3.1
Cholesterol	230	220	188	200	203	212	220	240	255	266
T. Protein	7.8	7.6	7.1	7.4	7.5	8.2	8.3	8.1	8.2	8.0
Albumin	4.0	4.5	4.0	4.1	4.1	4.4	4.3	4.6	4.6	4.3
T. Bilirubin	1.0	0.8	1.0	1.2	0.8	0.9	0.8	1.1	1.1	1.2
Alk. P'tase	65	47	65	70	67	87	107	80	65	73
LDH	155	208	179	195	212	195	180	180	185	172
SGOT	48	80	95	84	85	73	58	60	58	56

TABLE 4
Physiological Variation of Bicycling Biochemist Vs. Analytical Variation of SMA-12/60

	Physiological Variation	Analytical Variation	Ratio of Physiological to Analytical Variation
Calcium	0.46	0.12	3.8 times
Phosphorus	0.77	0.05	15. 4 times
Glucose	58 *	1	58.0 times*
BUN	3.6	0.4	9.0 times
Uric Acid	0.6	0.2	3.0 times
Cholesterol	25	10	2.5 times
T. Protein	0.4	0.2	2.0 times
Albumin	0.2	0.1	2.0 times
T. Bilirubin	0.16	0.05	3.2 times
Alk. P'tase	16	3	5.3 times
LDH	19	9	2.1 times
SGOT	15 †	7	2.1 times†

*Not a true physiological variation since patient is a diabetic.
†Not a true physiological variation since strenuous exercise can cause skeletal muscles to leak transaminase; and because diabetic and post-exercise ketosis causes false-positive SGOT elevations.

There. I've said it.

Said what? (1) That physiological variation should be considered in interpreting borderline abnormal tests; and (2) That some people will go to ridiculous lengths to prove a point.

Richard L. Reece, M.D.
Minneapolis, Minnesota

Acknowledgement: I should like to thank Doctor David Kvistberg for participating in this study.

Any pathologist wishing to contribute material for this section is invited to do so.

Meeting

Pediatric Day will be held March 11, 1972 at the Mayo Clinic. The program will be comprised of a series of talks given by the faculty relating to pediatric problems. Dr. Mary Ellen Avery, Professor and Chairman of the Department of Pediatrics, McGill University, will be the guest speaker and will talk on oxygen and mist therapy. For information, write: Dr. E. C. Burke, Mayo Clinic, Rochester, Minnesota 55901.

That which is striking and beautiful is not always good, but that which is good is always beautiful.—Ninon de L'Enclos



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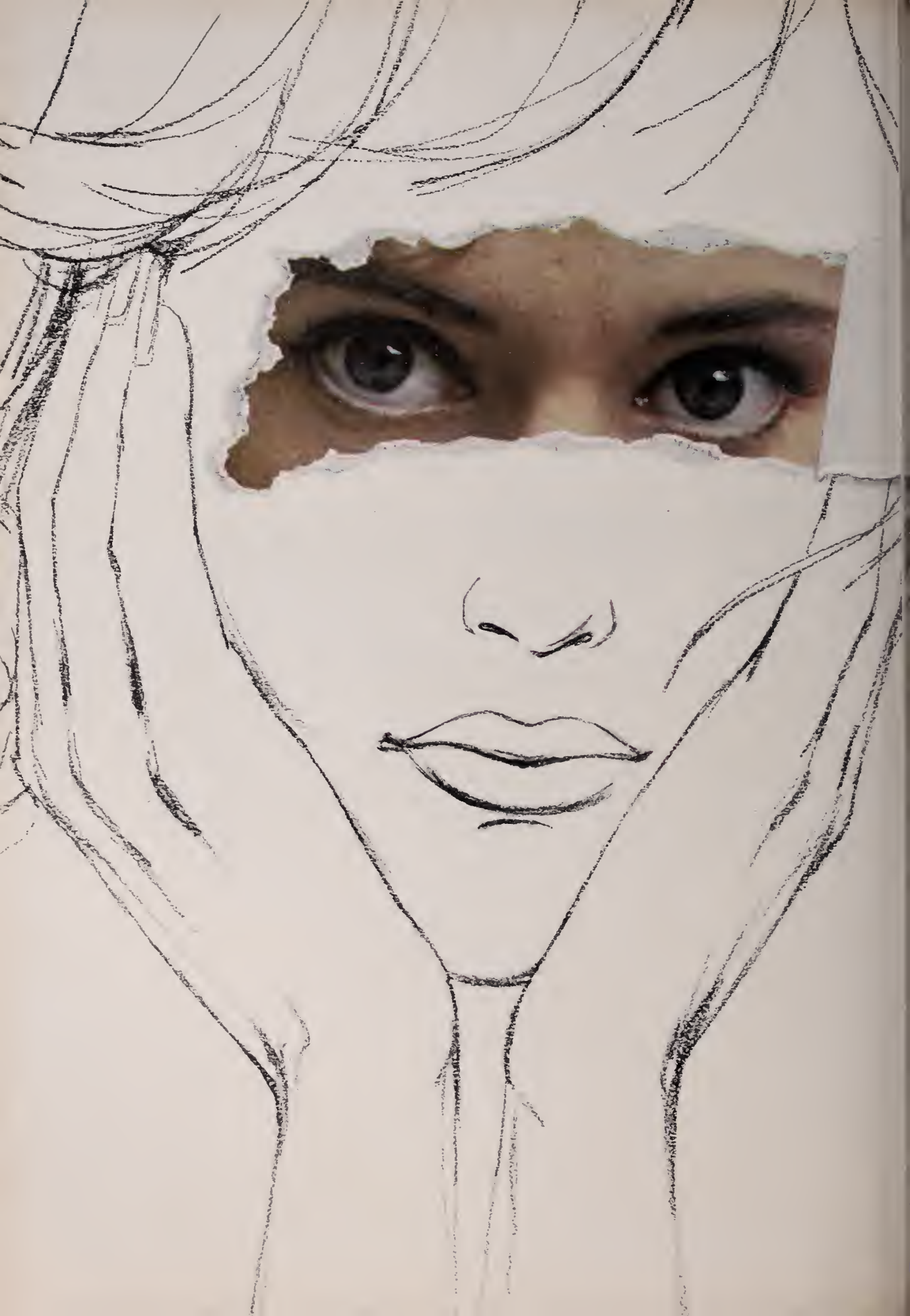
Indications: Peptic ulcer, gastroenteritis, pylorospasm, biliary dyskinesia, functional hypermotility and irritable colon.
Contraindications: Glaucoma, severe cardiac disease.
Precautions: Since varying degrees of urinary hesitancy may occur in elderly men with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug. Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.

Side Effects: The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

Dosage: The maximal tolerated dosage is usually the most effective. For most adult patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthine is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

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Warnings: *Drug Dependence:* Physical and psychological dependence and abuse have occurred. Chronic intoxication, from prolonged use and usually greater than recommended doses, leads to ataxia, slurred speech, vertigo. Carefully supervise dose and amounts prescribed, and avoid prolonged use, especially in alcoholics and addiction-prone persons. Sudden withdrawal after prolonged and excessive use may precipitate recurrence of pre-existing symptoms (e.g., anxiety, anorexia, insomnia) or withdrawal reactions (e.g., vomiting, ataxia, tremors, muscle twitching, confusional states, hallucinosis; rarely convulsive seizures, more likely in persons with CNS damage or pre-existent or latent convulsive disorders). Therefore, reduce dosage gradually (1-2 weeks) or substitute a short-acting barbiturate, than gradually withdraw. *Potentially Hazardous Tasks:* Driving a motor vehicle or operating machinery. *Additive Effects:* Possible additive effects between meprobamate, alcohol, and other CNS depressants or psychotropic drugs. *Pregnancy and Lactation:* Safe use not established; weigh potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential. Animal data at five times the maximum recommended human dose show reduction in litter size due to resorption. Meprobamate appears in umbilical cord blood at or near maternal plasma levels, and in breast milk at levels 2-4 times that of maternal plasma. *Children Under Six:* Drug not recommended.

Precautions: To avoid oversedation, use lowest effective dose, particularly in elderly and/or debilitated patients. Consider possibility of suicide attempts; dispense least amount of drug feasible at any one time. To avoid excess accumulation, use caution in patients with compromised liver or kidney function. Meprobamate may precipitate seizures in epileptics.

Adverse Reactions: *Central Nervous System:* Drowsiness, ataxia, dizziness, slurred speech, headache, vertigo, weakness, paresthesias, impairment of visual accommodation, euphoria, overstimulation, paradoxical excitement, fast EEG activity. *Gastrointestinal:* Nausea, vomiting, diarrhea. *Cardiovascular:* Palpitations, tachycardia, various forms of arrhythmia, transient ECG changes, syncope; also, hypotensive crises (including one fatal case). *Allergic or Idiosyncratic:* Usually after 1-4 doses. Milder reactions: itchy, urticarial, or erythematous maculopapular rash (generalized or confined to groin). Others: leukopenia, acute nonthrombocytopenic purpura, petechiae, ecchymoses, eosinophilia, peripheral edema, adenopathy, fever, fixed drug eruption with cross reaction to carisoprodol, and cross sensitivity between meprobamate/mebutamate and meprobamate/carbromal. More severe, rare hypersensitivity: hyperpyrexia, chills, angioneurotic edema, bronchospasm, oliguria, anuria, anaphylaxis, erythema multiforme, exfoliative dermatitis, stomatitis, proctitis, Stevens-Johnson syndrome; bullous dermatitis (one fatal case after meprobamate plus prednisolone). Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Hematologic:* Agranulocytosis and aplastic anemia (rarely fatal), but no causal relationship established. Rarely, thrombocytopenic purpura. *Other:* Exacerbation of porphyric symptoms.

Usual Adult Dosage: 1200 to 1600 mg daily, in three or four divided doses; doses above 2400 mg daily not recommended.

Overdosage: Suicidal attempts with meprobamate, alone or with alcohol or other CNS depressants or psychotropic drugs, have produced drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse, and death. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Meprobamate is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption.

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A Myopic Point of View

"Evans was extremely short-sighted, and a reluctant wearer of glasses. Without them, he could see small things held a few inches from his eyes in extraordinary detail, while everything else was a vague blur. Consequently the details he saw with microscopic exacitude, undistracted by the outside world, had a greater significance for him than for other men." (Evans, Joan. Time and Change: the story of Arthur Evans and his Forebears. London. 1943.)

SINCE THE EDITOR from time to time will comment on the medical scene, it might be well to establish the point of view from which these observations will be made. The point of view will be myopic for the reason that this is the natural state of the editor.

Myopia is a visual defect with many compensations. The fortunate victim carries with him a built-in magnifying glass that enables him to read the finest print with ease. All he needs do is whip off his glasses, and in my case I then have plus four diopter-stereo vision which roughly changes agate to pica type. In a theater darkened for the performance the less-gifted must strike a match to read the program. We myopes without spectacles simply bring the program closer, enlarge the image, and read.

Before the age of ten I knew that the only way to read the signs on the little clerestory-like window at the front end of a street-car was to run out into the street to get a closer view. An observant teacher put me in the front row, because I couldn't read the blackboard from the back of the room. When she found me leaving my front seat for a closer look, I was sent to the school nurse with the result, glasses.

Myopia to a degree is no handicap to a physician. He isn't required to see everything in perfect focus. For instance, a laboratory report may be that the fasting blood sugar is 120 mgm %. Anyone with good vision can read that the fasting blood sugar is 120 and, turning to his normal laboratory values, see that 60-100 is normal hence he is looking at an elevated fasting blood sugar. The myope can't see that well, hence he might question the elevation; can he trust his technician (or Technicon) for consistency of determination; has his laboratory been tested with unknowns against other laboratories; was his patient fasting when the nurses and laboratory technicians said he was? Or consider a change in a laboratory finding. A gastrointestinal bleeder comes in with a hemoglobin of 11.8 Gm/% and the following morning's reading is 11.5. Again the myope will have difficulty seeing the difference here, might ask the patient how he feels, observe the blood pressure, pulse, skin color, peer at the stool and ask for further hemoglobin readings only because knowing he has faulty vision, he needs more information than the sharper sighted.

I am recurrently amazed at the ability of my clear-sighted friends to see grade one Keith Wagner changes in the eye grounds after they find out what the high blood pressure reading is.

The myopic electrocardiographer is well advised to read his tracings with glasses, avoiding the magnification of unaided vision. He will be most helpful to the clinician if he focuses his blind spot on certain squiggles of the galvanometer: notches, detents, minute Q waves, microscopic S-T deviations. Again not having impeccable vision, he might read the chart or even (with the attending's consent) go over the patient. Finally, there is no better choice of investigator for a double-blind study than a myopic doctor.

The child who couldn't see "The Emporor's New Clothes"* obviously was severely myopic. One wonders what happened to him. With moderate negative lenses he might have grown up to make a fine physician.

Reuben Berman, M.D.
Minneapolis, Minnesota

*Fairy Tales, by Hans Christian Anderson Crown Publishers, New York. See also, Gross, F.: The Emperor's Clothes Syndrome. New Eng J Med 285:893. 1971. Spodick, D. H.: Ibid 285:1261.

Editorials

Female Sterilization

THE ARTICLE in this issue by Thorsteinsson and Pratt* gives a review of the more frequently used sterilization procedures over the past 50 years.

The Madlener technique has an unacceptable failure rate and is no longer used. Methods such as described by Irving and Uchida trade an increase in operating time, blood loss and technical difficulty for a questionably lower failure rate as compared to the simple Pomeroy procedure.

The vaginal approach increases the failure rate in all the types of procedures and has a higher postoperative febrile morbidity. In addition, a certain number of cases will begin vaginally, but cannot be completed because adhesions prevent the fallopian tubes from being brought into the field.

The variation described in the article on the "Pratt Operation" appears significantly more time consuming, technically more difficult, and with a greater chance of blood loss since the tube is wedged out of the cornu of the uterus. No statistics on the number of times the procedure was done nor on the failure and complication rate are given in the article.

Currently I favor the following two approaches. In the immediate postpartum period, a very small incision is made at the inferior edge of the umbilicus and the tubes are ligated and divided by the Pomeroy technique using plain catgut. The total operating time is approximately twenty minutes and the reported failure rate is 0.3%.[1]

Virtually all our interval sterilizations are now being done by the laparoscopic technique recently described in this Journal.[2] Contrary to the statement in the article by Thorsteinsson and Pratt, a section of fallopian tube is removed by the laparoscopic biopsy forceps for definite histologic and legal evidence of interruption.

Richard P. Bendel, M.D.†
Minneapolis, Minnesota

*See page 204.
†Assistant Professor, Department of Obstetrics and Gynecology, University of Minnesota, Minneapolis.

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Subcutaneous Emphysema in Obstetrics*

INTRAPARTUM EMPHYSEMA is a rare disease, so unusual that an individual with an active practice in Obstetrics and Gynecology, will probably never diagnose such a patient unless he is unusually alert to the syndrome. The great variation in frequency observed from one in 200 deliveries to one in 100,000 is probably due to the minor degrees of emphysema reported in the former, and to severe disabling degrees in the latter. What is surprising, after reading the paper of Ebrahimi and Prem,* is not that intrapartum emphysema does occur, but that it does not occur in much greater numbers than we presently realize. The most likely explanation for intrapartum emphysema is "the violent strain of childbirth." This enormous intra-abdominal pressure is also manifested the next day or so following delivery in the rather prominent conjunctival hemorrhages we have all observed in some parturients. Yet hemorrhages in the eyegrounds are more commonly noted than subcutaneous emphysema. Other factors thus must be involved in intrapartum emphysema, possibly congenital weakness in one or more pulmonary alveoli. The disease is self limited, not lethal and the treatment consists of supportive measures. It must be differentiated from preeclampsia which can have a fatal outcome if not discovered.

Howard M. Levine, M.D.
Minneapolis, Minnesota

*See page 991 of the December issue 1971 of Minnesota Medicine.

Erratum

The February President's Letter stated 225 medical students would begin medical training in Minnesota in September, 1972. This should read: 225 students will begin medical training in Minneapolis, 40 in Rochester and 24 in Duluth.

Chemotherapy by Arterial Infusion

In Carcinoma of the Liver

EXTENSIVE METASTATIC DISEASE involving the liver responds poorly to systemic chemotherapy. Direct arterial infusion, however, is a valuable form of palliation. The techniques of intra-arterial infusion of localized malignant disease have been extensively studied recently and perfected. Techniques in use today vary from long-term continuous therapy with the Chronofusor to the relatively simple Fenwald pressure bag system. As reported in the paper by Doctors Fortuny, Theologides and Kennedy in this issue,* a variety of tumors may be treated with palliative benefit by these techniques. Many of their patients did not exhibit prolonged survival when compared to other members of the study group, but the quality of their survival was greatly enhanced in those persons who respond to the treatment.

As would be expected, those tumors which respond to intra-arterial infusion by means of the hepatic artery are those which have known response to the drug. Tumors which tend to be refractory to the drug being utilized normally would not be expected to respond and, indeed, most often do not even with the higher dosage achieved by means of direct arterial infusion. Carcinomas of the colon, pancreas and biliary tract are known to be responsive in some degree to systemic 5-fluorouracil and FUDR (deoxy-uridine) therapy. Likewise carcinoma of the breast is known to be a responder to fluorinated pyrimidine therapy. Hepatic metastatic disease from tumors primary in these organs can be expected to be responsive to intra-arterial infusion in a significant number of cases. The results are often dramatic in reduction in size of massively enlarged livers, disappearance of jaundice, and return of appetite and activity levels approaching, or reaching normal. With a good initial response to arterial infusion through the hepatic artery in metastatic carcinoma of the liver, one may attempt to maintain such responses by periodic systemic maintenance therapy with the same drug utilized for infusion. This is oftentimes effective for a long time and when breakthrough occurs, secondary infusion therapy can achieve remission. Should a case prove refractory to systemic maintenance therapy periodic reinfusion by means of the hepatic artery can be used to maintain the remission.

Although selective catheterization of the desired artery may be accomplished percutaneously, it is my experience that surgical placement of the catheter under direct vision is to be preferred over percutaneous placement. The anatomic variations known to exist within the arterial supply to the liver and biliary tree make it difficult to achieve isolated placement of the infusion catheter in the hepatic artery and dislodgment, as noted in the article mentioned, is common. The degree of systemic toxicity manifested during arterial infusion may well be related to the placement of the catheter since a dislodged catheter may present a fair amount of drug unaltered to the system without passage through the liver. If the patient is a satisfactory surgical candidate, the performance of a laparotomy to place the infusion catheter is justified and presents a permanent form of placement which allows reinfusion without a second manipulative procedure. The authors' point is well taken that appropriate equipment for placement of an infusion catheter should be present at the time of laparotomy for suspected carcinomas of the colon, biliary tract or pancreas. Obviously the risk of laparotomy is greater than that of percutaneous placement of the catheter but with careful technique the complication rate is low and the risk justified. In colon carcinoma where venous seeding of the liver is found at the time of primary operation and minimal disease is left following resection of the primary tumor, placement of an infusion catheter at the time of original laparotomy is advisable. Similarly in cases of pancreatic and biliary tract carcinoma the placement of the infusion catheter at the time of initial laparotomy is preferable when primary resection for cure is not possible. A second laparotomy for catheter placement or the manipulation of percutaneous catheter placement is thus avoided and the patient has a correctly placed catheter available for infusion therapy.

The modern surgeon must bear in mind not only primary treatment, but must also be aware of the methods of palliative management in the patient who is not resectable for cure. This again emphasizes the desirability of the team approach

See page 197.

n oncology with early communication between the arious disciplines involved when tumor manage- nent is considered.

The complications of arterial infusion therapy f the liver are minimal when careful observation nd laboratory controls are used. The toxic man- festations of fluorinated pyrimidines when used y direct arterial infusion are similar to those een with systemic therapy. Appropriate moni- oring by means of white blood count and platelet evels plus serum transaminase and lactic dehydro- enase levels will avoid undue problems. Stomati- is, diarrhea, and systemic toxic symptoms even- ually prescnt themselves in most cases if the nfusion is carried out for a long enough period. Close observation of serum enzymes and bilirubin evels must be maintained in the jaundiced patient n whom the infusate can be hepatotoxic. In such patient, the SGOT and LDH levels should prob- bly be monitored daily and any significant eleva- ion would indicate either the necessity to reduce he dosage of infusate or to discontinue the infusate or a period of time. Tolerance to infusion is greater with the catheter securely placed in the iepatic artery.

Patients being treated by percutaneously placed r surgically placed catheters may be treated as utpatients. The Fenwald system can be used for mbulatory infusion as well as the Chronofusor ystem. An active intelligent patient can be taught o change the infusion bag in the Fenwald system and with the smaller Fenwald bag, the patient may be restricted in little, if any, of his activities. Percutaneous catheterization through the arterial system of the upper extremity is more satisfactory for ambulatory infusion by the Fenwald system than by the femoral route.

Intra-arterial infusion of carcinoma involving the liver by means of hepatic artery cannulation is practical and effective. Palliation is achieved in a significant number of patients who would otherwise be unlikely responders to chemotherapeutic management. Fluorinated pyrimidines for such therapy are well established, undue toxicity is not encountered when the patient is carefully monitored by means of clinical and laboratory means. Although surgical placement of the infusion catheter is to be preferred as regards exact placement and lack of dislodgment, percutaneous catheterization is an accepted method. Catheter dislodgment occurs with percutaneous catheterization but replacement is simple in experienced hands. Ambulatory infusion is a practical method and can be accomplished with the Fenwald closed system or Chronofusor techniques. Palliation produced by this treatment is worthwhile and should be considered also when systemic chemotherapy is unsuccessful. Anticipation of such infusion should be a part of the surgeon's approach to suspected primary cases of carcinoma of the colon, biliary tree and pancreas and when indicated, the catheter placed at the time of the original laparotomy.

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It was all very well to say "Drink me," but the wise little Alice was not going to do *that* in a hurry. "No, I'll look first," she said, "and see whether it's marked '*poison*' or not"; for she had read several nice little stories about children who had got burnt, and eaten up by wild beasts, and other unpleasant things, all because they *would* not remember the simple rules their friends had taught them: such as, that a red-hot poker will burn you if you hold it too long; and that, if you cut your finger *very* deeply with a knife, it usually bleeds; and she had never forgotten that, if you drink much from a bottle marked "poison," it is almost certain to disagree with you sooner or later.*

*Lewis Carroll's "Alice in Wonderland."

Case Report

Anterior Mediastinal Teratoids

An Unusual Case of Bilateral Mediastinal Tumors

S. K. IMES, M.D.* AND W. F. HOOK, M.D.*

IF WE EXCEPT LYMPHOMATA, which may be considered multicentric in origin, teratoids are the most common of all primary tumors of midanterior mediastinal origin.[3] Rusley[4] in an exhaustive review, analyzed all the mediastinal teratoid tumors in the world literature through 1939, adding six cases of his own, for a total of 245 cases. Numerous other reports have been published since.

Maier[2] reported unusual features in four patients with mediastinal teratoids. One patient presented with bilateral mediastinal tumors. Another rapidly developed tumor extension, inoperability, and widespread metastases after having been considered for several years as having an innocent dermoid because of peripheral calcification.

A search of the literature has failed to reveal other radiologic reports of multiple mediastinal teratoids; although small satellite lesions, not in direct communication with the main teratoid, have been reported in at least one instance in the surgical literature.[1] This report documents a second case of separate large bilateral midanterior mediastinal teratoid tumors discovered radiologically.

Case Report

A white male, age 58, was referred to the Radiology Department with complaints of upper abdominal distress associated with substernal pain and burning (heartburn), and moderate difficulty with urination. His blood pressure and physical findings were normal, with the exception of an enlarged prostate.

Radiographic Findings

Intravenous pyelography was normal with the exception of an enlarged prostate deforming the base of the urinary bladder and producing mild post voiding bladder retention. The cholecystographic study was normal. An upper gastrointestinal series revealed a moderately large sliding hiatus hernia with associated stress regurgitation of gastric contents into the esophagus.

Chest fluoroscopy and roentgenograms outlined what appeared to be three roughly spherical tumor masses in the midanterior mediastinum varying in size from four to seven centimeters in diameter. Peripheral calcification was present in all three masses. The smallest mass was seen nearly exactly in the midsagittal plane and approximately four centimeters deep to the sternum. The largest mass was situated more anteriorly, overlapped the midline, and protruded moderately into the right chest. The third mass lay slightly further posteriorly and projected into the left chect (Figures 1, 2, 3). Transmitted pulsatory movement was seen, particularly in the posterior left tumor. No fat fluid levels could be found and no bone or teeth were present. The chest study was otherwise radiologically normal. The radiologic diagnosis was dermoid tumor, either a multiple or a large single multilobated dermoid extending to both right and left sides of the mediastinum.

Laboratory studies demonstrated the hemoglobin to be 13.3 grams percent, the white blood count 5,700 with a normal differential, urinalysis normal, blood urea nitrogen 18.5 milligrams percent. The electrocardiogram was normal. Transurethral resection of the enlarged prostate had been done on December 13, 1966.



Fig. 1—Posterior anterior chest.

*Department of Radiology, Quain and Ramstad Clinic, Bismarck, North Dakota.



Fig. 2—Lateral chest.

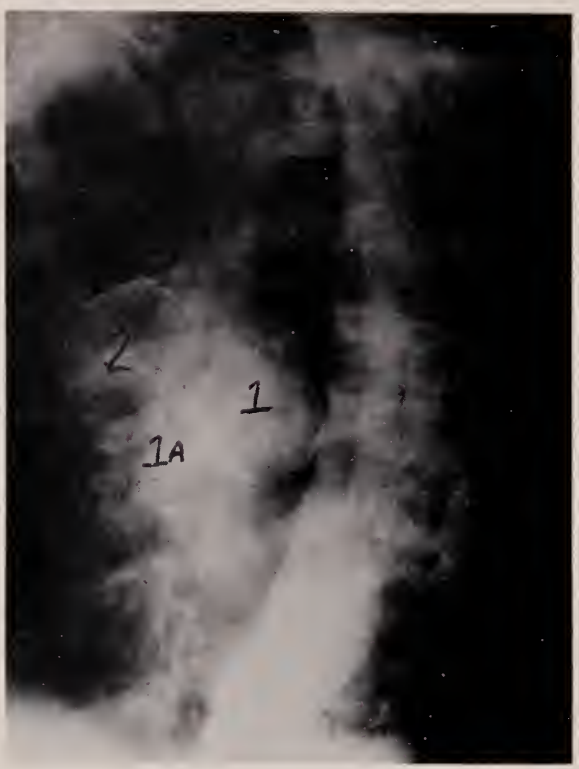


Fig. 3—Left anterior oblique chest.

Operative Findings

Mediastinal exploration was done on January 20, 1967, through a sternal splitting incision. Two separate mediastinal masses were encountered and removed by sharp and blunt dissection. Both masses were intimately adherent to the pleura, but mediastinal in origin. It was necessary to open the pleura to resect the masses. The bulk of the left mass projected posteriorly and bulged into the left chest, with a smaller lobe that projected into the midline area giving rise to the radiologic impression of a third smaller midline tumor. The pericardium was not involved. The bulk of the right tumor mass lay in the right mediastinum and bulged into the right chest. Microscopic pathologic diagnosis of both tumor masses was that of dermoid tumor without evidence of malignancy.

Summary

Teratoid tumor of the midanterior mediastinum is not rare, but apparently rarely present as more than a single lesion. Radiographs of only one such case were readily found in the literature. This report documents the radiologic discovery of a second case of bilateral separate midanterior mediastinal teratoid tumors. The left mediastinal tumor had a lobate extension in the midmediastinum, giving the radiographic appearance of a third tumor mass. Both tumors were surgically excised; microscopically both were diagnosed as benign dermoids.

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Erratum

Dr. David E. Dines' editorial "Bronchial Asthma" in the February issue* stated that the Humidified oxygen should be administered in a concentration to raise the $PaCO_2$ to 60mm. of mercury. This should read "raise the PaO_2."

*Page 125.

Anesthesia*

Meigs, Professor of Midwifery at Jefferson Medical College (1841-1861), was markedly antagonistic to anesthesia in obstetrics, as noted by S. Weir Mitchell while a student at Jefferson in the late 1840's:

> "My father first in Philadelphia used ether in childbed. Professor Meigs violently opposed it and one day undertook to show its peril to a class of three hundred or more at Jefferson Medical School. A big billy goat was brought into the arena, which was called the bull ring, and Ellerolie Wallace, Dr. Meig's assistant, gave the ether. At last, Professor Meigs announced the demise of Billy, and the corpse was taken out and left in a small room at the halfway landing of the main stairway. The lecture over, we were noisily descending to the chemical lecture when Wallace opened the door to Billy's room. Out came Billy, very drunk, charged between Wallace's long legs into a mass of delighted students, and Billy and students went downstairs in one wild confusion. My father was never weary of inquiring of his colleague after this patient's health."

Despite this experience, Meigs retained his beliefs. Hodge, Professor of Midwifery at Pennsylvania (1835-1869), wrote in 1866:

> "Professor Meigs has strong protests against anaesthesia in labor, declaring that it is fraught with danger and predicting that, in the course of a few years, it will be banished from practice, except in a few extraordinary cases."

Van S. Lawrence,, M.D.†
Minneapolis, Minnesota

*Anesthesia from Colonial Times, James E. Eckenhoff, BS, MD, FFARCS, J. B. Lippincott Company—1966.
†Chief of Anesthesiology, Mt. Siani Hospital.

The harvest of old age is the recollection and abundance of blessings previously secured.—Cicero's "De Senectute".

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Six medical student at the University of Minnesota have received Student Achievement Awards worth $1,000 each for academic excellence, student leadership and community service.

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evertheless, Lincocin should be used
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nificant allergies.

patients with impaired renal function,
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dney function. Its safety in
egnant patients and in infants
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Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatme *Skin and mucous membranes*—Skin rash urticaria, vaginitis, and rare instances of e foliative and vesiculobullous dermatitis ha been reported. *Liver*—Although no direct r lationship to liver dysfunction is establishe jaundice and abnormal liver function te (particularly serum transaminase) have be observed in a few instances. *Cardiovascul* —Instances of hypotension following pare teral administration have been reporte particularly after too rapid IV administr tion. Rare instances of cardiopulmonary a rest have been reported after too rapid I administration. If 4.0 grams or more admi istered IV, dilute in 500 ml of fluid a administer no faster than 100 ml per hou *Special senses*—Tinnitus and vertigo ha been reported occasionally. *Local reactio* —Excellent local tolerance demonstrated intramuscularly administered Lincoc (lincomycin hydrochloride). Reports of pa following injection have been infrequen Intravenous administration of Lincocin 250 to 500 ml of 5% glucose in distille water or normal saline has produced n local irritation or phlebitis.

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Review

Acute Renal Failure

Indications for Dialysis

HENRY T. SMITH, M.D.*

ACUTE RENAL FAILURE is defined as the sudden development of impaired renal function from any of a number of medical and surgical conditions. It is usually accompanied by oliguria, i.e., output of less than 500cc per day, but azotemia may develop in the face of normal urine volume.[1] The standard renal failure regimen (fluid restriction, protein restriction, etc.) carries a distressing mortality rate (40-50%)—with infection being the most common cause of death. The use of peritoneal dialysis and hemodialysis has produced justifiable optimism for the management of these patients. However, these techniques do not supplant the more conservative measures; they merely supplement these measures. A common question is: "At what stage in the management of acute renal failure should one augment the conservative approach with dialysis?" It is the purpose of this paper to discuss some of the guidelines used in answering this question.

Indications

Indications for dialysis in acute renal failure are listed in Table 1. The development of the uremic syndrome (Table 2) in these patients is a clear indication for dialysis. Although the toxic substance or substances producing the syndrome have not yet been determined, the dramatic response to dialysis strongly suggests that many of the manifestations are due to a circulating dialyzable material.

Onset of Clinical Uremia

It is no longer considered satisfactory medical practice, however, to await or indeed to permit the development of uremia. In a review of this problem in 1963, Balslov and Jurgensen[2] noted that until 1960 the indications for dialysis were the onset of clinical uremia, or a serum urea level greater than 400 mgm per 100 ml, as well as symptomatic hyperkalemia and/or severe disturbances in other serum electrolytes. In 1960 Teschan[3] advanced the concept of "prophylactic dialysis" with the aim of dialyzing patients before the development of clinical uremia. His daily treatment of military patients produced such encouraging results that it initiated an almost universal trend toward early dialysis, so that severe clinical symptomatology and chemical abnormalities due to renal failure are rarely seen in many major centers. It was thought that early or prophylactic dialysis would reduce the morbidity and mortality associated with acute renal failure.

TABLE 1
Indications for dialysis in acute renal failure.

1. Uremic syndrome
2. BUN > 125-150mgm%
3. Rapidly rising BUN (> 30mgm% per day)
4. Marked fluid retention
5. Marked chemical distortion
6. Drug intoxication

TABLE 2
Uremic Syndrome

Gastrointestinal manifestations	Anorexia Nausea Vomiting Constipation or diarrhea Melena Mucosal ulcerations
Neuromuscular manifestations	Lethargy Apathy Mental Confusion Delusions Muscular twitching Peripheral neuropathy Convulsions
Cardiopulmonary manifestations	Pericarditis Overhydration Hypertension
Miscellaneous	Anemia Azotemia Acidosis Hyponatremia Hyperphosphatemia Hypocalcemia Hyperkalemia

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These patients would thus be permitted to convalesce uneventfully from the precipitating disease or injury, with diet and activity restricted only by the underlying disease. With this regimen a significant improvement in wound healing was also noted: an observation substantiated experimentally in dogs. Nayman[4] reported that renal failure had no effect upon *healed* wounds in these animals, but uremia induced in the first five days of wound *healing* caused disruption in every case. After nine days wound healing was not affected. Early and regular hemodialysis prevented wound breakdown when renal failure was induced immediately after laparotomy.

It is impractical to consider daily dialysis in most clinical situations because of limited machinery and personnel. Therefore, some reasonable parameters—short of clinical uremia—are needed.

BUN (125-150mgm%)

Fischer et al.[5] in a retrospective study, noted a decrease in the mortality rate from 77% to 51% when dialysis was instituted to maintain the blood urea nitrogen below 150mgm%. Parsons et al.[6] found that the mortality rate fell from 88% to 25% if dialysis was used when the blood urea nitrogen reached 120-150mgm%. Scribner[7] has noted a similar improvement (69% to 26%) if early dialysis was utilized. It seems, therefore, that a blood urea nitrogen between 125mgm% and 150 mgm% represents a reasonable indication for dialysis, even if the patient's clinical condition is still satisfactory. This guideline, however, is not incontrovertible; many patients will recover uneventfully with conservative therapy after reaching this level. Neverthless, the bulk of the medical literature supports this suggestion as a reasonable approach. If there are signs of uremia prior to this level, then earlier dialysis may be necessary. This practice of earlier and more frequent dialysis has reduced mortality to 8-36% in those dialysis centers using vigorous preventive dialysis.[8]

The rate of rise of the blood urea nitrogen varies from patient to patient with conservative therapy. In a well managed patient this rate should not exceed 20mgm% per day. A rate in excess of 20-30mgm% per day provides warning of the need to prepare for dialysis or arrange transfer of the patient to a center that can provide dialysis.

Chemical Abnormalities

Other indications for dialysis in acute renal failure include fluid overload and various chemical abnormalities, such as metabolic acidosis. Because of the marked effectiveness of the cation exchange resins, hyperkalemia is generally not considered an indication for dialysis. It is always important to attempt to establish the etiology of the renal failure, because certain drugs and toxins require dialysis before the development of any of the aforementioned signs.[9]

Peritoneal Dialysis vs. Hemodialysis

The choice between peritoneal dialysis and hemodialysis depends primarily upon the availability of equipment, as well as the interests and experiences of the physicians managing the patient. Peritoneal dialysis can remove any metabolic product that can be removed by hemodialysis, although it requires about four times as long to achieve the same chemical improvement. There are no absolute contraindications to peritoneal dialysis, but there are a few relative contraindications, e.g., peritonitis or recent abdominal surgery. However, there are reports of peritoneal dialysis being instituted hours after repair of a perforated peptic ulcer, and within a week after appendectomy without harm. It has also been suggested that peritoneal irrigation might indeed be of value in the therapy of generalized peritonitis.[10]

Summary

The indications for dialysis have been broadened during the past decade in that an attempt has been made to prevent the development of the uremic syndrome and maintain the patient in an optimum condition while he recovers from his primary illness. Ideally there would be no restrictions regarding food and fluids, but expenses and limited equipment and personnel dictate the need for reasonable restrictions. Early and frequent dialysis is used to maintain the blood urea nitrogen less than 150mgm%. Dialysis is also necessary if conservative management results in a rate of rise in the blood urea nitrogen that is greater than 20mgm% per day. The improvement in morbidity and mortality attest to the wisdom of this approach.

Dr. John Merrill[11] has summarized the overall approach to dialysis in acute renal failure:

"The prime indication for treatment with the artificial kidney continues to be that first suggested by Abel, i.e., to maintain life and reasonable well-being during periods of acute renal insufficiency where the underlying lesion is reversible. The development of our understanding of the general therapeutic problems of acute renal failure has progressed to the point where the artificial kidney, in many cases, is unnecessary for the treatment of this syndrome. Under no circumstances should one entertain the concept that the artificial kidney is a substitute for good conservative management."

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Cardiopulmonary Schistosomiasis Syndrome

This syndrome consists of cardiac or pulmonary symptoms caused by bilharzic infestation of the lungs secondary to *Schistosoma mansoni* in the intestinal tract or *S. haematobium* in the urinary tract. The presence of *Schistosoma* in the lungs was recognized as early as 1885. Sorour in 1928 described the pathologic lesions these parasites produce in pulmonary tissues. In the Near East the condition is common and is a recognized cause of right-sided heart failure. Males are more frequently affected than females. Age incidence is usually between 12 and 35 years.

The local pathologic lesions are those of obliterative pulmonary arteriolitis, produced by lodging of the ova in the arteriolar wall. A sufficient number of such lesions causes dilatation of the main pulmonary artery and hypertrophy of the right ventricle. Roentgenograms show fine, diffuse mottling as well as mitral configuration of the heart. An outstanding difference between Ayerza's syndrome, which is characterized by intense cyanosis, and cardiopulmonary schistosomiasis is that in the latter condition cyanosis occurs only terminally. Other diseases that may stimulate bilharzic cor pulmonale are rheumatic mitral insufficiency, patient ductus arteriosus, and patent interauricular septum. Antimony is a specific therapeutic agent in *Schistosoma* infestation; however, as this drug may exert a toxic effect upon the myocardium, its intensive use in this combined cardiopulmonary syndrome is contraindicated.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

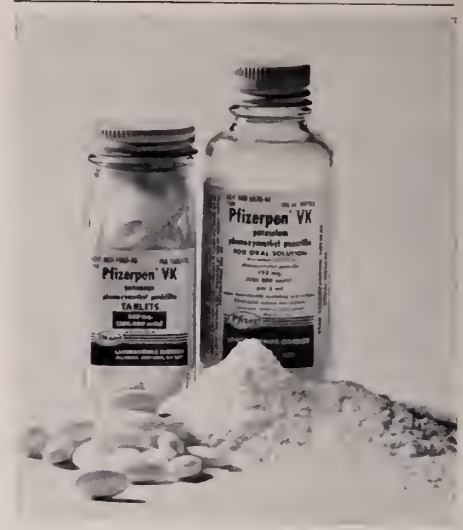


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Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

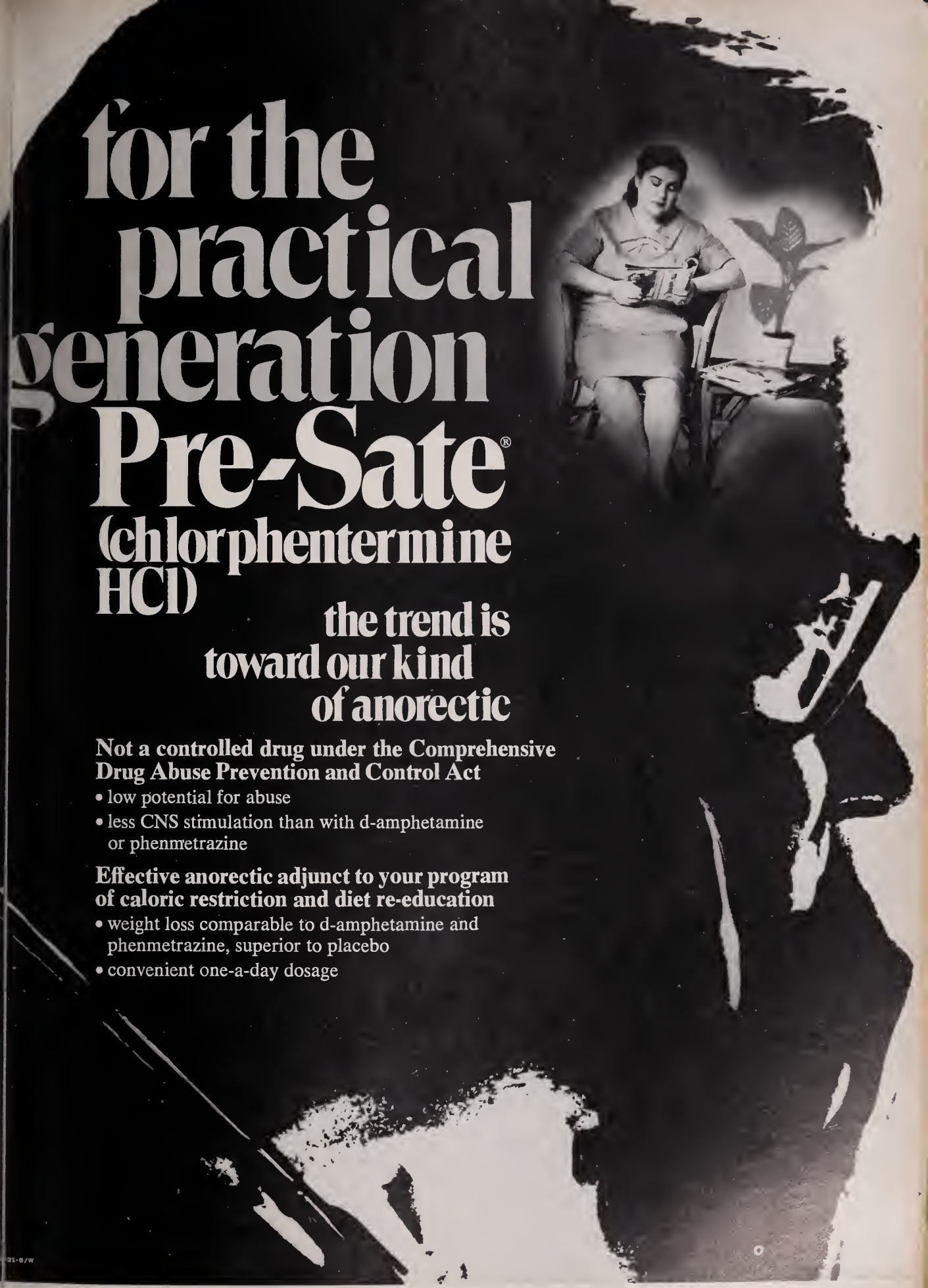
Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

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INDICATIONS: Useful in the management of depression, both acute (reactive) and chronic; particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination; also useful for management of depression and associated anxiety accompanying or related to organic illnesses.
CONTRAINDICATIONS: Benactyzine hydrochloride: Glaucoma and previous allergic or idiosyncratic reactions to benactyzine hydrochloride or related compounds. **Meprobamate:** Acute intermittent porphyria and allergic or idiosyncratic reactions to meprobamate or related compounds such as carisoprodol, mebutamate, tybamate, carbromal.
WARNINGS: The following information on meprobamate pertains to 'Deprol' (meprobamate + benactyzine hydrochloride): **Meprobamate:** *Drug Dependence:* Physical and psychological dependence and abuse have occurred. Chronic intoxication, from prolonged use and usually greater than recommended doses, leads to ataxia, slurred speech, vertigo. Carefully supervise dose and amounts prescribed, and avoid prolonged use, especially in alcoholics and addiction-prone persons. Sudden withdrawal after prolonged and excessive use may precipitate recurrence of pre-existing symptoms (e.g., anxiety, anorexia, insomnia) or withdrawal reactions (e.g., vomiting, ataxia, tremors, muscle twitching, confusional states, hallucinosis; rarely convulsive seizures, more likely in persons with CNS damage or pre-existent or latent convulsive disorders). Therefore, reduce dosage gradually (1-2 weeks) or substitute a short-acting barbiturate, then gradually withdraw. *Potentially Hazardous Tasks:* D... a motor vehicle or operating machinery. *Additive Effects:* Possibl... tive effects between meprobamate, alcohol, and other CNS depre... or psychotropic drugs. *Pregnancy and Lactation:* Safe use not estab... weigh potential benefits against potential hazards in pregnancy, n... mothers, or women of childbearing potential. Animal data at five ... the maximum recommended human dose show reduction in litte... due to resorption. Meprobamate appears in umbilical cord blood ... near maternal plasma levels, and in breast milk at levels 2-4 time ... of maternal plasma. *Children Under Six:* Drug not recommended.
PRECAUTIONS: Meprobamate: To avoid oversedation, use lowest ... tive dose, particularly in elderly and/or debilitated patients. Conside... sibility of suicide attempts; dispense least amount of drug feasible ... one time. To avoid excess accumulation, use caution in patients wit... promised liver or kidney function. Meprobamate may precipitate se... in epileptics.
ADVERSE REACTIONS: Nausea, dry mouth, other g.i. symptoms ... cope; one case each of severe nervousness and loss of power of co... tration. The following side effects, which have occurred after administr... of its components alone, have either occurred or might occur whe... combination is taken. **Benactyzine hydrochloride:** Benactyzine h... chloride alone, particularly in high dosage, may produce dizziness, th... blocking, a sense of depersonalization, aggravation of anxiety, or ...

When mild depression and associated anxiety interfere with living

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ace of sleep patterns, and a subjective feeling of muscle relaxation. ere may also be anticholinergic effects such as blurred vision, dryness mouth, or failure of visual accommodation. Other reported side effects e included gastric distress, allergic response, ataxia, and euphoria. **probamate:** *Central Nervous System:* Drowsiness, ataxia, dizziness, rred speech, headache, vertigo, weakness, paresthesias, impairment of ual accommodation, euphoria, overstimulation, paradoxical excite- nt, fast EEG activity. *Gastrointestinal:* Nausea, vomiting, diarrhea. *Car- vascular:* Palpitations, tachycardia, various forms of arrhythmia, tran- nt ECG changes, syncope; also, hypotensive crises (including one fatal se). *Allergic or Idiosyncratic:* Usually after 1-4 doses. Milder reactions: ny, urticarial, or erythematous maculopapular rash (generalized or nfined to groin). Others: leukopenia, acute nonthrombocytopenic pur- ra, petechiae, ecchymoses, eosinophilia, peripheral edema, adenopa- , fever, fixed drug eruption with cross reaction to carisoprodol, and ss sensitivity between meprobamate/mebutamate and meprobamate/ bromal. More severe, rare hypersensitivity: hyperpyrexia, chills, angio- urotic edema, bronchospasm, oliguria, anuria, anaphylaxis, erythema ltiforme, exfoliative dermatitis, stomatitis, proctitis, Stevens-Johnson ndrome; bullous dermatitis (one fatal case after meprobamate plus ednisolone). Stop drug, treat symptomatically (e.g., possible use of nephrine, antihistamines, and in severe cases corticosteroids). *Hema- ogic:* Agranulocytosis and aplastic anemia (rarely fatal), but no causal relationship established. Rarely, thrombocytopenic purpura. *Other:* Exacerbation of porphyric symptoms.

USUAL ADULT DOSAGE: One tablet three or four times daily, which may be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended.

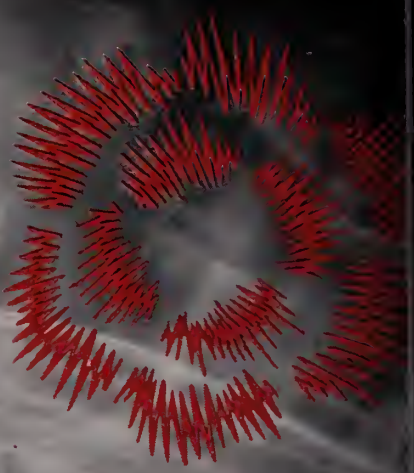
OVERDOSAGE: Overdosage of 'Deprol' (meprobamate + benactyzine hydrochloride) has not differed substantially from meprobamate overdosage: **Meprobamate:** Suicidal attempts with meprobamate, alone or with alcohol or other CNS depressants or psychotropic drugs, have produced drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse, and death. Empty stomach, treat symptomatically, cautiously give respiratory assistance, CNS stimulants, pressor agent, as needed. Meprobamate is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully. Careful monitor urinary output; avoid overhydration; observe for possible re[illegible] to incomplete gastric emptying and delayed absorption.

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Warnings: *Idiosyncratic Reactions:* Rarely, first dose has been followed by extreme weakness, transient quadriplegia, dizziness, ataxia, temporary vision loss, diplopia, mydriasis, dysarthria, agitation, euphoria, confusion, disorientation. Symptoms usually subside during the next several hours. Supportive and symptomatic therapy, including hospitalization, may be necessary. *Pregnancy and Lactation:* Safe use not established; weigh potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential. *Children Under Five:* Drug not recommended. *Potentially Hazardous Tasks:* Driving a motor vehicle or operating machinery. *Additive Effects:* Possible additive effects between carisoprodol, alcohol, and other CNS depressants or psychotropic drugs. *Drug Dependence:* Use cautiously in addiction-prone patients.

Precautions: To avoid excess accumulation, use caution in patients with compromised liver or kidney function.

Adverse Reactions: *Central Nervous System:* Drowsiness, dizziness, vertigo, ataxia, tremor, agitation, irritability, headache, depressive reactions, syncope, insomnia. *Allergic or Idiosyncratic:* Usually seen after 1-4 doses in patients not previously exposed, e.g., rash, erythema multiforme, pruritus, eosinophilia, fixed drug

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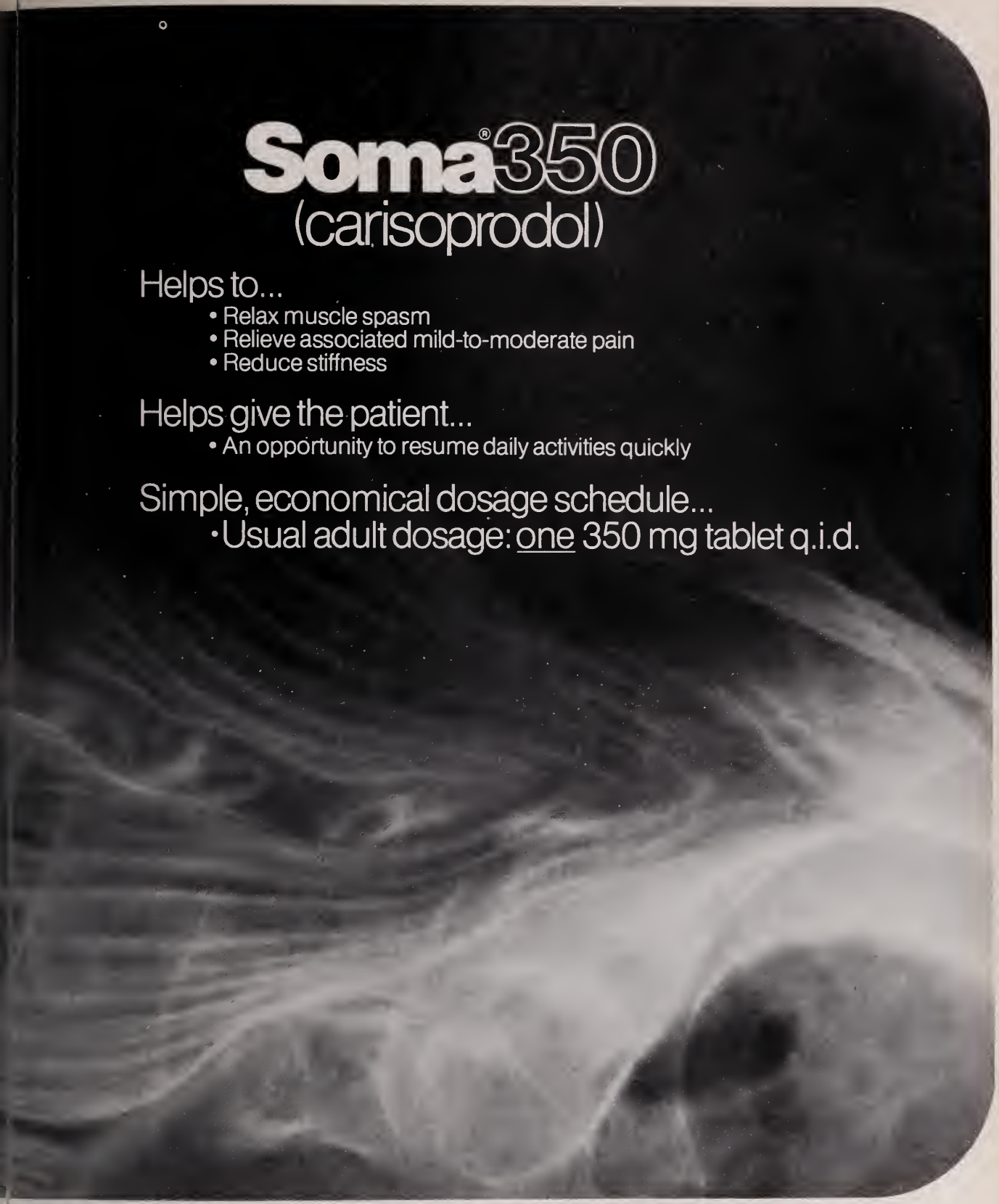
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Simple, economical dosage schedule...

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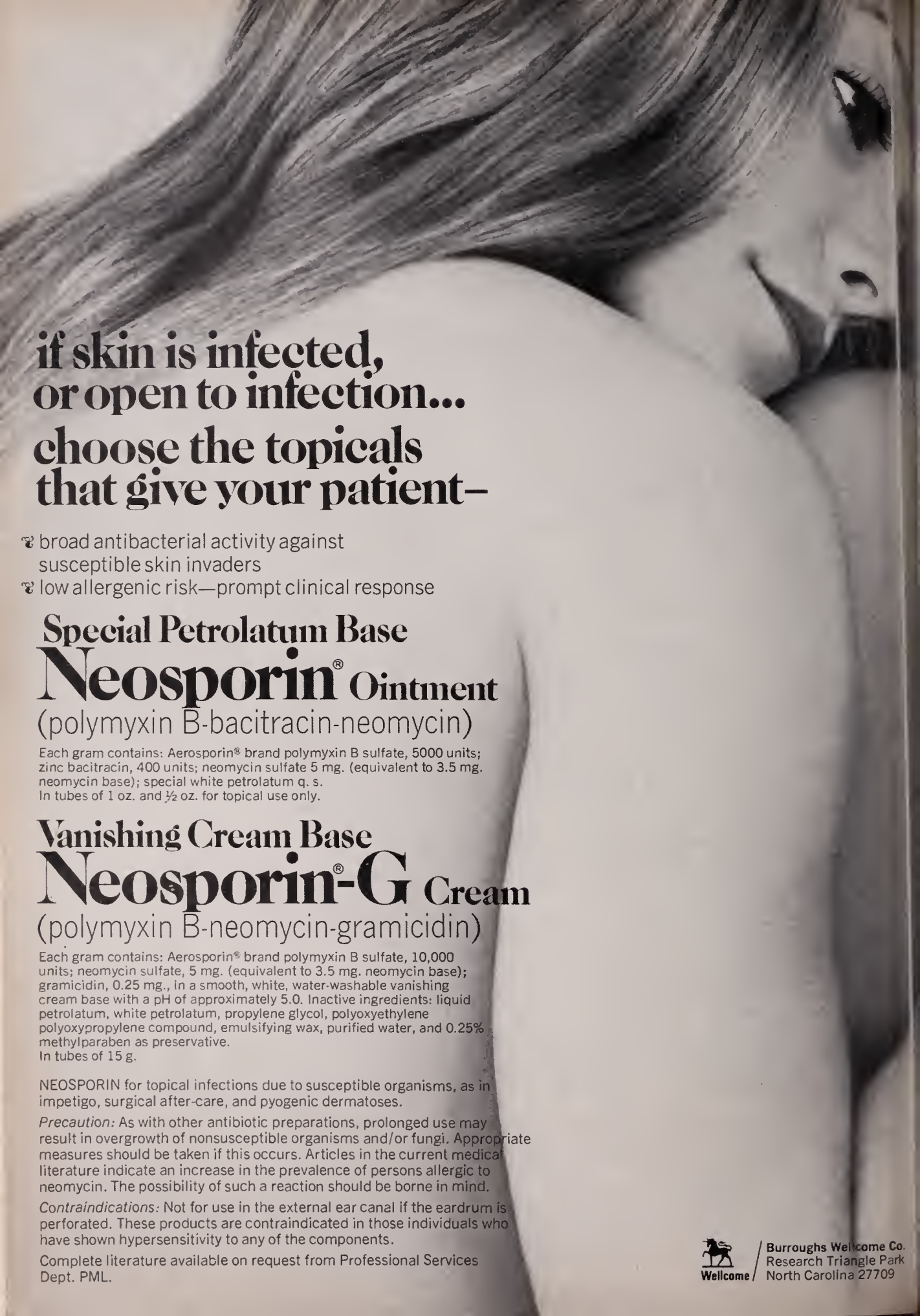


eruption with cross reaction to meprobamate. More severe manifestations: asthma, fever, weakness, dizziness, angioneurotic edema, smarting eyes, hypotension, anaphylactoid shock. Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Cardiovascular:* Tachycardia, postural hypotension, facial flushing. *Gastrointestinal:* Nausea, vomiting, hiccup, epigastric distress. *Hematologic:* Leukopenia and pancytopenia (on carisoprodol plus other drugs).

Usual Adult Dosage: One 350 mg tablet three times daily and at bedtime.

Overdosage: Has produced stupor, coma, shock, respiratory depression, and, very rarely, death. Overdosage of carisoprodol plus alcohol or other CNS depressants or psychotropic drugs can be additive. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Carisoprodol is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully with related drug meprobamate. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption. REV. 10/71

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The Thalamic Pain Syndrome

THOMAS R. SMITH, M.D.*

THE THALAMIC PAIN syndrome was first described in 1906 by Dejerine and Roussy[4] whose description is still felt to be the most reliable. The most prominent features of this disorder include:

Clinical Manifestations

Continuous pain on the side contralateral to the thalamic lesion, usually described as varying from an ache, to a boring, gnawing, burning, icy or crushing sensation.[11] The trunk is often the site of such pain, but the limbs are not spared.[6] The pain may be increased by sensory stimuli such as intense light, loud noises, penetrating odors, cold water hitting the skin, seeing water or taking a drink. Widespread and diverse vasomotor and other autonomic disorders are associated with the pain. It is refractory to analgesics of all types, including morphine. In this respect, the sensation is similar to causalgia. When approached, the patient become fearful and shows a grimacing or withdrawal out of proportion to the degree of the applied stimulus.

Sensory

Paroxyms of hypersensitivity to sensory stimulation occur sometimes of such severity as to prevent the clinician from doing an adequate sensory examination. Usually slight elevation of the sensory threshold for selected sensory modalities also occur. Upon painful stimulation, the sensation is referred widely around the point of stimulation. Stimulation with heat, cold, pain or touch leads to a more unpleasant sensation than is found using the same stimulus in an unaffected area. There is a longer delay between the time of stimulation and when it is appreciated. The pain brought about by a certain stimulus may persist and far outlast the duration of stimulation.

Motor

A severe motor deficite is often lacking; the presence of severe paresis actually argues against the painful condition of thalamic origin,[4,11] although mild hemiparesis is common.

Other signs and symptoms are less constantly seen in this syndrome. Caudal thalamic lesions may extend rostrally and lead to dissociated movements of the face. The lower part of the face on the contralateral side may remain immobile as a mask when the patient laughs or cries, but contracts readily with volitional movements. The loss of emotional expression may be due to interruption of the reflex pathway extending from the thalamus to subcortical or extrapyramidal nuclei. The reverse reaction is seen in some cases with internal capsular hemiplegia: an inability to perform voluntary facial movement with preservation of the ability to smile.[2,6]

*Neurology Service, Minneapolis Veterans Hospital.

Faulty Localization

The disturbances of sensibility on the contralateral side of the body are manifest primarily by ataxia, astereognosis, diminished two-point discrimination,[2] and faulty localization of various sensory stimuli, which is felt to arise from involvement of thalamic nuclei which relay to the parietal cortex. There is tactile inattention, manifest in its most severe form by amerognosia in which the involved arm or arm and leg are ignored. Amerognosia is the sensory counterpart of anosognosia which is unawareness of hemiparesis. An identical syndrome may occur in lesions confined to the parietal lobe.[6] In the thalamic syndrome there is also decreased appreciation of posture and passive movement which leads to a decreased weight appreciation on the affected side. Stereognosis is decreased because of defects in touch, pressure and position.[2]

Dyskinesia

The ataxia, greater in the upper than the lower extremities, may be due to sensory losses or disruption of the cerebellorubrothalamic connections. Muscle tone may be diminished, but slight spasticity is found associated with mild hemiparesis due to involvement of part of the internal capsule by lateral spread of the lesion. The thalamus is close to the pallidum and, in the thalamic syndrome, involuntary movement of a choreoathetoid nature is often seen and tends to be more marked in the upper extremity. An intention tremor of large amplitude may result from disruption of rubrothalamic connections.

In vascular lesions of the thalamoperforating arteries, one encounters

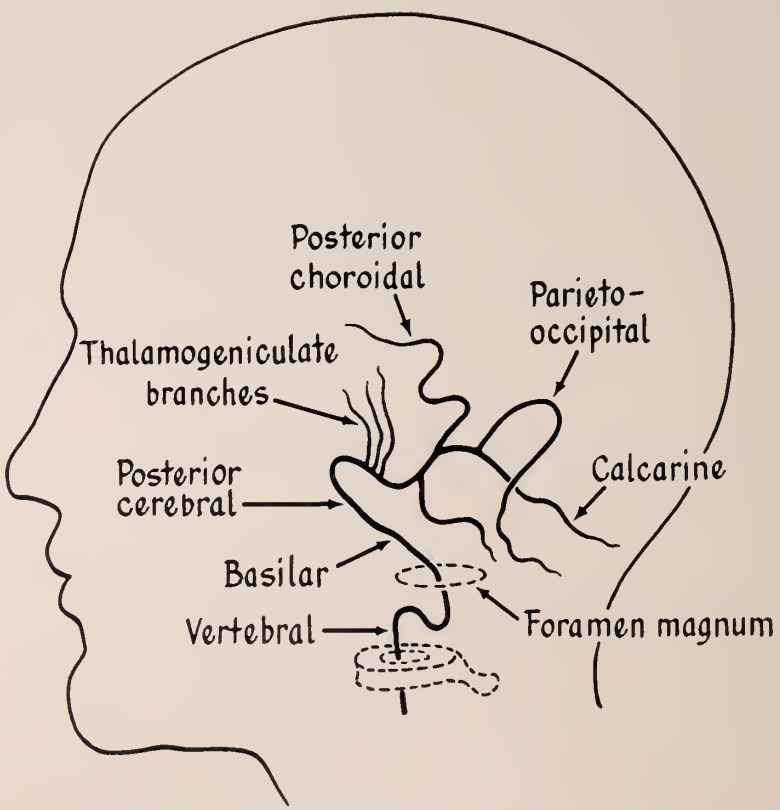


Figure 1

ataxia and involuntary movements of the opposite upper limb with the fingers and hand frozen in a choreoathetoid posture. If vascular lesions affect the pulvinar, and especially the lateral geniculate body, homonymous quadrantic or hemianoptic defects will be found in the contralateral visual fields.[2]

Physiologic Considerations

There are a number of physiologic considerations in understanding the thalamic pain syndrome. Dejerine and Roussy believed that the lesions causing thalamic pain resulted from occlusion of the thalamogeniculate artery, which is a branch of the posterior cerebral artery (Figure 1) and supplies the posterolateral portion of the thalamus, the anterior part of the pulvinar and the geniculate bodies.[2] Head[5] and others found softening of the posterolateral thalamus alone in patients who had had the classic thalamic syndrome.

Vascular

Conditions which may give rise to thalamic lesions include hypertension, arteriosclerotic disease, embolization, luetic arteritis, intracranial aneurysms and arteriovenous malformations. Neoplasms rarely produce the thalamic syndrome. Symptoms very similar to the thalamic pain syndrome may result from many other lesions, including lesions of peripheral nerves, the spinal cord, medulla, midbrain and the parietal region of the cortex.[11]

Nerve

Experimental and clinical investigations have led investigators to the fol-

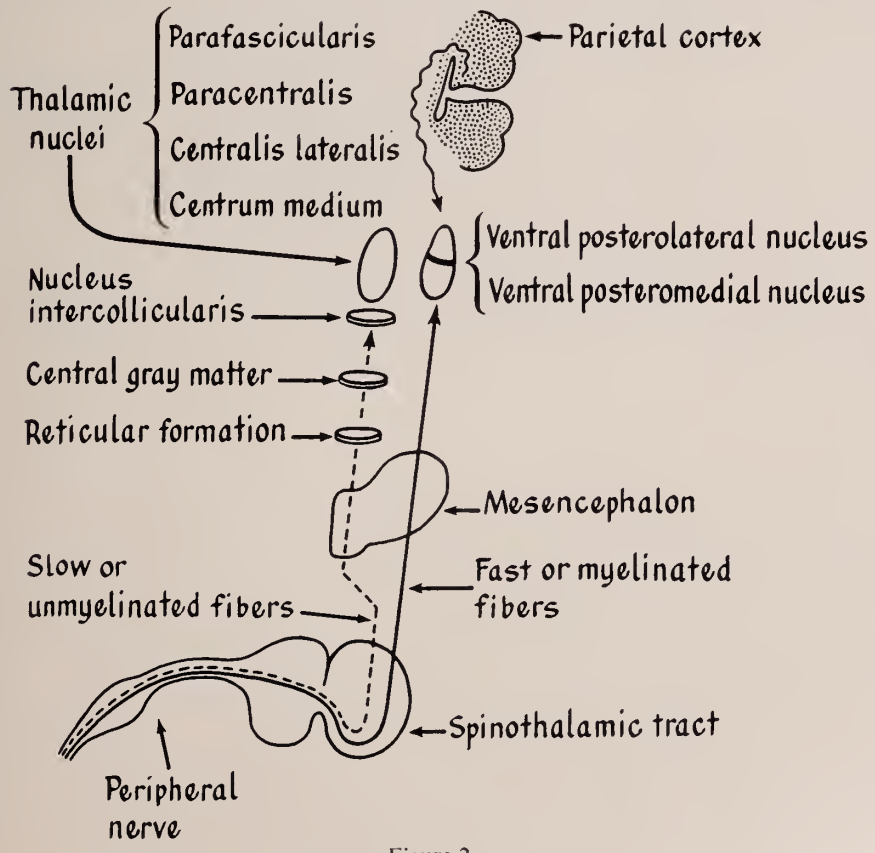


Figure 2

lowing conclusion regarding the physiology and mechanisms of thalamic pain:

There are two systems serving pain function. One is the slow or extralemniscal or paleospinothalamic; the other is the fast or lemniscal or neospinothalamic system[11] (Figure 2).

Slow pain is mediated over high-threshold, fine, unmyelinated fibers less than 2 microns in diameter to the medial or paleothalamus, at rates of 0.6 to 2.0 m/sec. Slow pain is usually described as a disagreeable burning, gnawing or boring sensation. These fine unmyelinated fibers are intermingled with the large, myelinated, fast pain fibers in the peripheral nerves and spinothalamic tract of the spinal cord. The unmyelinated fibers course through the reticular formation and, via polysynaptic pathways, through central gray matter to nucleus intercollicularis. From this site they reach the parafascicularis, paracentralis and centralis lateralis thalamic nuclei.[11] Lesions in the parafascicularis and interlaminar nuclei lead to relief of thalamic pain with only minimal or no sensory loss.[11]

Fast pain is mediated over myelinated fibers 2-4 microns in diameter at rates of 10 m/sec. These fibers have a lower threshold. This type of pain is sharply circumscribed as to location and type of stimulus and is less disagreeable than slow pain. The fast pain fibers are also intermingled in the peripheral nerves and spinothalamic tract of the spinal cord but course to the mesencephalon and thence to the ventral posterolateral nucleus of the thalamus. Lesions in the ventral posterolateral or the ventral posteromedial nucleus lead to inability to circumscribe an area of pain or other sensation, but the pain is perceived over a poorly defined area.

Evidence of slow and fast pain systems has led investigators to the conclusion that the fast pain system exercises some control or suppression mechanism over the slow pain system under normal circumstances. It is felt that the impulses from the ventral posterolateral nucleus exert an inhibitory effect on the slow pain system at the level of the medial thalamus (centrum medium and parafascicularis). The loss of input from either the periphery or cortex to the ventral posterolateral nucleus or a lesion in the ventral posterolateral nucleus can cause the thalamic pain syndrome.[11] Recent investigation has also suggested that lesions in the mesencephalon may give rise to painful sensations which may account for spontaneous paroxysms of pain. Inhibitory feedback from the cortex and thalamus may be abolished and give rise to hyperesthesia.[10]

Treatment

Thalamic pain is resistant to therapy. Some patients find relief with the use of a tranquilizing drug (phenothiazines) with diphenylhydantoin or carbamazepine plus supportive psychotherapy. Neurosurgical approaches for this type of pain have led to the interruption of the fibers in the supraclaustral area leading from the thalmus to the postcentral gyrus. This procedure avoids the hyperpathia and dysesthesia which sometimes appear after operations on the mesencephalon or thalamus. The operation is very difficult and endangers important motor and sensory pathways; transient motor and sensory deficits may occur following surgery. About 4% of these patients develop hemiparesis or ataxia postoperatively and 3% show dysesthesia and hyperesthesia. The mortality of stereotaxic thalamotomy varies from 2 to 7.5%. Therefore this type of treatment is reserved only for those who are resistant to all other approaches. Complete or nearly complete pain

relief is attained in 70% of patients undergoing surgery, but there is a 50% recurrence of the pain over a period of months to years. When a strong emotional component is present, Spiegel and Wycis[1] recommend a mesencephalothalomotomy with removal of the dorsal medial nucleus of the thalamus as well as interruption of the pathway to the postcentral gyrus. Some surgeons have treated patients by producing lesions in other thalamic nuclei. Mark et al.[8,9] found lesions of the ventral posterolateral or the ventral posteromedial nucleus led to loss of the ability to circumscribe the area of pain; but these patients continued to have a diffuse burning type pain. Lesions in the parafascicularis and intralaminar nuclei, on the other hand, produced pain relief without sensory deficits.[7,8,9]

Conclusion

The thalamic pain syndrome is a disagreeable burning sensation on the side contralateral to a thalamic lesion. The destruction is usually secondary to thrombosis of the thalamogeniculate artery, or branches leading to it. The pain sensation results when impulses mediated by the fine unmyelinated slow-conducted fibers are uninhibited. These impulses are normally inhibited by fibers from the ventral posterolateral and ventral posteromedial nuclei, the termini of large, well myelinated fast-conducting pain fibers.

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Family Practice

Clinical Decision Making*

Some Practical Problems and Theoretical Considerations

DAVID SPENCER, M.D.

Benjamin Johnson has said that, "If all possible objections to a project are first overcome, no project will ever be undertaken". In a sense this comment is apropos to clinical decision making and an analysis of clinical judgment. In attempting to develop information concerning clinical judgment with a view towards developing a teaching methodology to encompass this subject, it becomes evident that there are certain characteristics of good judgment which can be delineated and, hopefully, can be taught.

Clinical Set

One of the tools which we will be applying to this kind of study will be that of set theory.[1] One of the concepts which we feel is helpful is the idea of a clinical set. We might define a clinical set as a given number of patients who have signs and symptoms which can be measured and quantified in such a way that they can all be described as having the same clinical problem. This is saying that they suffer from the same disease except it implies that we define the signs and symptoms arbitrarily which we will use to define this disease entity in a given group of patients. One of the problems which good clinicians have appreciated for centuries is that disease as such may have a spectrum of manifestations, a spectrum of signs and symptoms, and that precise identification of a disease at a given time can be an extremely difficult process.

An example of this might be to talk about carcinoma of the prostate without carefully defining what signs and symptoms you identify as being diagnostic of this disease. A nodule in one lobe as opposed to low back pain from widespread dissemination could lead to great differences in clinical decision making in terms of treatment, operative procedures, drug applications, morbidity, disability or mortality studies. As an example of a disease upon which a clinical spectrum might easily be agreed upon, the simple problem of nosebleed was chosen.

Nosebleed Problem

In analyzing the problem of nosebleed, we felt that some degree of agreement could be reached as to the presence or absence of a distinguishing sign (i.e., visible bleeding). Bleeding is a hallmark that all clinicians accept as evidence of the disease. This may been so elementary as to be humorous, but it is a concept which is essential to decision making.

The analysis of the nosebleed problem requires identification of the various decision points with respect to treatment and identification of all options for treatment which lead to the various outcomes associated with this medical problem. A flow diagram is useful to chart the decision process involved in treating nosebleed. We found it useful to start our analysis at the earliest possible time (with respect to the natural history of the disease process) at which a contact between physician and patient could occur. This was judged to be the telephone contact which very frequently results in the initial treatment decision made by the physician.

The physician might ascertain at this point answers to some or all of the questions listed in Table 1 before making a decision as to seeing the patient at the hospital, recommending self treatment at home, or recommending an office call. In terms of attempting to quantify the amount of bleeding in order to decide between home treatment, office call or hospital, he might apply the criterion prescribed in Table 2. Assuming that the physician felt that the patient could achieve control of bleeding with home treatment, he would decide against either an office visit or hospitaliza-

*Outgrowth of a seminar held in the Department of Family Practice and Community Health, University of Minnesota, Minneapolis, directed by Dr. Vernon Weckwerth as principle discussant and Dr. Ben Fuller as Chairman of the Department. Mr. Clyde Neu, Eric Dardinger and the author prepared this paper as an extension of this seminar.

ion. If bleeding continued, he would be faced with . second decision (decision No. 2). At this point e might obtain additional information pertinent o this particular nosebleed. Let us then assume hat the physician feels an office call is indicated. Vhen the physician sees the patient in the office, e is faced with a decision which we refer to in he flow diagram (Figure) as decision 3.

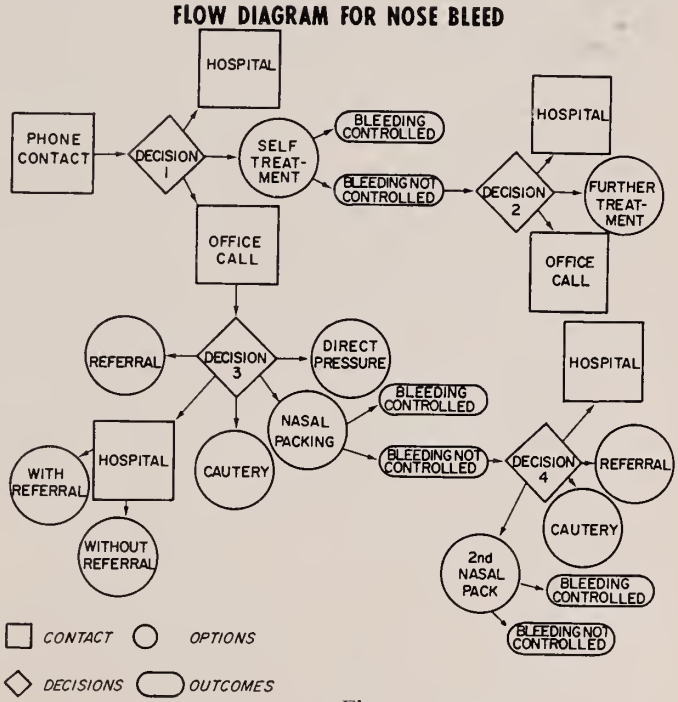
TABLE 1
Clinical Data Base for Nosebleed

1. Is this the first episode of nosebleed?
2. Is this the first time the patient has phoned?
3. How old is the patient—older than age 65?
4. Has any treatment been attempted?
5. Has there been any trauma or bone breakage?
6. Has the patient had a previous episode in last 30 days?
7. Is the patient able to make a judgment concerning duration and amount of flow?
8. Is the patient taking any medicine (anticoagulants)?
9. Does the patient suffer from any other serious disease?
10. Does the patient have any disturbance in coagulation?
11. Is the patient or a parent unusually anxious about the bleeding?
12. Has the climate or season of the year or recent URI predisposed to bleeding?

Some of the options at decision 3 that the physician has available are outlined in the flow diagram. Let us next assume that he chooses the option of nasal packing. The outcome from that decision may be that the bleeding is controlled or hat the bleeding is not controlled. If not controlled, he is faced with decision 4 and again with number of options for treatment. By applying he flow diagram and the decision tables to the reatment of a very common problem such as osebleed, we are able to follow the pathway of he logic of the physician in handling this particular nosebleed. By this kind of analysis, it is hoped hat we will be able to follow the pathway of the decision logic which the student or resident exercise in the given clinical situation. We hope that ltimately we may be able to establish probabilities and outcomes on the various pathways, so hat we can teach some idea of the best and most logical pathway and perhaps the most successful pathway from the standpoint of problem solving.

When we review the problem of nosebleed, it points to the fact that much of the medical literature is written without careful consideration as to the natural history of the problem, or the exact point at which the problem is encountered by the clinician. Hence, we are able to find papers advocating as treatment of nosebleed application of nasel packing in all instances,[2] the absolute avoidance of nasal packing in all but a very few instances, controlled hypotension,[3] injection of lidocaine with epinephrine[4] or the ligation of the external carotid artery or the ophthalmic arteries.[5]

In attempting to teach correct therapy, one can see that it is essential that a clear statement of the etiology, duration, severity and many other clinical factors should be made. Too often, the discernment of this information which has to be the basis of decision making has been left to the judgment of the student. If his only experience base has been in an emergency room or in an



Figure

TABLE 2
Decision Criterion—Duration and Flow of Bleeding

Duration of Bleeding	Under ½ hr	½-1 hr	1-2 hr	2-8 hr	Over 8 hr
Flow: Maximum	Home	Home	Office	Office	Hospital
Moderate	Home	Office	Office	Hospital	Hospital
Excessive	Office	Office	Hospital	Hospital	Hospital

Combination of duration and flow measures indicates whether patient is to be treated at home, in the office, or in the hospital. Minimum bleeding is an intermittent and light flow. Moderate bleeding is a continuous but light flow. Excessive bleeding is a continuous and heavy flow.

ENT clinic, it is obvious his ability to make effective decisions about a given clinical encounter would be markedly limited.

Before the clinician can be expected to make an appropriate decision as to the treatment of nosebleed, it is easy to see that we must teach something about the total set: the natural history of nosebleed, the total number of nosebleeds that a clinician as a primary physician might be expected to encounter, the percentage of those that follow a pathway other than the expected course of prompt subsiding of bleeding with the natural control mechanisms. If we can teach something of the natural history of this clinical problem, it will be much simpler for the student to make good decisions concerning the treatment of nosebleed. This example may seem so completely obvious as to be trivial to most of the readers of this paper. However, as we look at the educational task confronting us as we teach clinicians, particularly in the area of family practice, it becomes obvious that methods, frameworks and displays of decision processes have to be made available to the student during his training period.

Let us just cite one other example that points to this need for model decision making. Our group in discussing medical decision making attempted to tackle the problem of peptic ulcer disease; taking a group of five clinicians with a total experience base of approximately 75 years. We were unable to discuss the issue of peptic ulcer until we separated the entity of peptic ulcer disease into at least two component parts, that of gastric and duodenal. Once we had carefully identified which one of these two conditions we were talking about, it was easy for us to proceed along a decision pathway.

A simple question in treating ulcer disease is whether or not a follow-up xray is necessary. This question in terms of peptic ulcer disease is unanswerable; in terms of gastric ulcer, the answer is yes; in terms of duodenal ulcer, the answer is considerably less absolute. It may depend upon the success of the therapy, the psychological attitude of the patient, his conformity to the treatment regimen and many, many other variables. It would appear that much of our literature dealing with peptic ulcer disease serves a pointless and useless purpose in that clinical decision making to be meaningful has to be based among other factors on the position of the ulcer.

This is but one example of the myriad of clinical problems in which a knowledge of the natu history of the disease process and careful eval tion as to whether that disease represents a sin clinical set or is part of a continuum of a clini problem will be extremely helpful. In the train of the medical student towards fruitful decisi making, the point is that by developing models decisions in which we show an optimal resoluti of a clinical problem or an optimal treatment f a given disease process perhaps we can teach method of problem solving. Perhaps we can al markedly refine our ability to delineate precis clinical problems and place them in such sets categorize them in such ways that data relating the decisions that have been made concerni treatment of these processes can be stored, r trieved, and analyzed retrospectively.

It may seem ridiculous to the experienced clir cian to say that treatment of nosebleed in eve instance demands packing. Yet, if the only set patients with nosebleeds that the clinician se are those referred to a specialty clinic, packir may be the most appropriate approach. Certainl were we able to clearly outline the total spectru of many common diseases and to clearly ascerta the natural history of these diseases, the proble confronting the primary physician would be mark edly simplified.

One of the clear problems that is evident i much of medical literature today is that the pr ary physicians who are on the first line of contac in many of the very common clinical diseases ha been unable to write or to collect data in a mean ingful way so as to make it available for teachin or for analysis by students who are training t move into areas of primary care. This failure i part of the breakdown of dialogue between th clinician and the specialist in modern medicine Certainly any system of problem analysis whicl will help the student to relate to this difference o background and difference of understanding o sets of common diseases would be extremely help ful as a teaching and learning mechanism. It i for this reason that our Department has been in terested in pursuing the possibility of this kind o data acquisition and the development of a mode towards teaching clinical decision making. Hope fully, then, some of what is referred to as the ar of medicine, the mystique of a competent primary physician, may be brought into a teachable, analyzable, scientifically oriented spectrum wherein students may be as intrigued and enthused as were our predecessors in watching the Oslers and Plummers of their time.

See page 269 for references.

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1 332S (2876)

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prescribing information appears on next page

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Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg., phenylephrine HCl, 15 mg., phenylpropanolamine HCl, 15 mg

Dimetapp Extentabs®

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PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics, sedatives, tranquilizers, etc.
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HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

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Clinical Decision Making—Spencer (Page 264)

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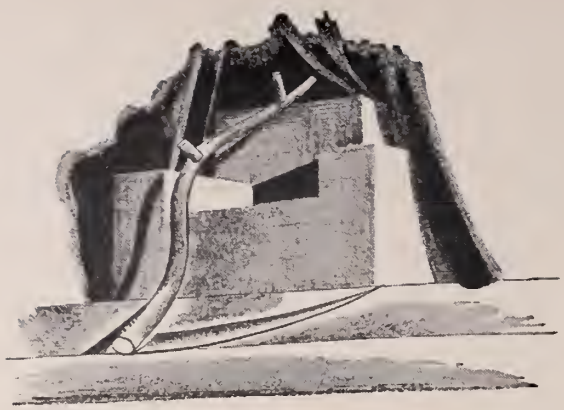
Soul

All my Care its self employes,
That to preserve, which me destroys:
Contrain'd not only to indure
Diseases, but, what's worse, the Cure:
And ready oft the Port to gain,
Am Shipwrackt into Health again.*

Body

But Physick yet could never reach
The Maladies Thou me dost teach;
Whom first the Cramp of Hope does Tear:
And then the Palsie Shakes of Fear.
The Pestilence of Love does heat:
Or Hatred's hidden Ulcer eat.
Joy's chearful Madness does perplex:
Or Sorrow's other Madness vex.*

*Andrew Marvell: A Dialogue Between the Soul and the Body. Lines 25-38, 1681.



In Memoriam

Earth has no sorrow that heaven cannot heal.—Moore

ARCHABALD L. ARENDS, M.D.

Dr. Archabald L. Arends, 89, Minneapolis physician died November 11. A graduate of Northwestern University Medical School, Dr. Arends first practiced at Casselton, North Dakota.

He was a member of the American Medical Association and the Hennepin County Medical Society and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Arends is survived by his wife, Evelyn.

MILTON H. SEIFERT, M.D.

Dr. Milton H. Seifert, Sr., who practiced medicine in the Lake Minnetonka area for 35 years, died November 13. He was 67. He began the Seifert Clinic in Excelsior in 1930, the year after graduating from the University of Minnesota Medical School.

He was a member of the Hennepin County Medical Society, the American Medical Association and an Associate Member of the Minnesota State Medical Association.

Dr. Seifert is survived by a daughter, Mary, and six sons, three of whom are physicians, Doctors Milton H. Seifert, Jr., Gregory L. Seifert and John D. Seifert.

RICHARD P. NEARY, M.D.

Dr. Richard P. Neary, 63, Minneapolis physician died November 6. He was head physician in the Outpatient Services Department of St. Mary's Hospital and a former president of the Hospital's Medical Staff. He had been in general practice for 38 years and on the St. Mary's staff for 20 years. A graduate of the University of Minnesota Medical School, Dr. Neary interned at Hennepin County General Hospital.

He was a Fellow in the American Academy of General Practice, a member of the Minnesota State Medical Association, the American Medical Association, the Hennepin County Medical Society and the American Association of Railroad Surgeons.

He is survived by his wife, Winifred, three daughters and three sons, one of whom is Dr. Michael Neary.

NICHOLAS F. MUSACHIO, M.D.

Dr. Nicholas F. Musachio, 59, physician at the University of Minnesota Health Service, died September 16. Dr. Musachio formerly served as chief of staff of St. Cloud Hospital and as president of the Stearns-Benton County Medical Society.

A graduate of the University of Minnesota Medical School, Dr. Musachio was also a former president of the Benton County Tuberculosis and Health Association, local surgeon for the Great Northern Railway, member of the Stearns-Benton County Medical Society, the Minnesota State Medical Association, the American Medical Association, the American Academy of General Practice and the American Geriatric Society.

Dr. Musachio is survived by his wife, Phyllis, five daughters and a son.

MALCOLM B. HANSON, M.D.

Dr. Malcolm B. Hanson, 73, Minneapolis radiologist, died September 1. A graduate of the University of Cincinnati College of Medicine, Dr. Hanson started practicing in Minnesota in 1937.

He was a member of the Hennepin County Medical Society and the American Medical Association and an Associate Member of the Minnesota State Medical Association.

Dr. Hanson is survived by his wife, Josephine.

LOUIS R. KOLLER, M.D.

Dr. Louis Koller, 81, ear, nose and throat specialist for over 50 years, died December 4. He continued to practice medicine until his death.

A graduate of St. Louis University Medical School, Dr. Koller was a member of the American Academy of Ophthalmology and Otolaryngology, American College of Surgeons, Hennepin County Medical Society and the American Medical Association. He was a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Koller is survived by his wife, Emilie, sons, Dr. Robert Koller of Minnetonka and John of Albuquerque and daughters Donna and Mrs. Joan Kongsvik, Jr.

MELVIN P. BAKEN, M.D.

Dr. Melvin P. Baken, Sr., 77, who was a practicing physician in Minneapolis for 50 years, died November 28. He was the former chief of staff at Fairview Hospital.

He was a member of the American College of Obstetrics and Gynecology, Minnesota Obstetrics and Gynecological Society, the American Medical Association and the Hennepin County Medical Society. Dr. Baken was also a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Baken is survived by his two sons, Richard J and Dr. Melvin P. Baken, Jr. of Edina.

Alcoholism

R. O. HEILMAN, M.D.*

MEDICAL SCIENCE now recognizes that alcoholism is a form of drug dependency. Symptoms can be recognized early, before the actual observation of the person's attitudes and behavior when drinking. It is generally accepted that how often a person drinks or how much he drinks are unreliable indexes for determining the existence or the non-existence of alcoholism. The crucial factor in recognizing an alcoholic, and especially the younger alcoholic, is how he uses alcohol. Generally, male alcoholics develop an alcoholic drinking pattern within three years after their first experience with "getting high." This is also true for 70% of the alcohol-addicted women. Other addictive agents result in psychological habituation and physical addiction in a much more rapid fashion; this is probably part of the reason that physicians have been slow in recognizing some of the early symptoms of alcoholism.

From experience in alcoholic treatment centers, psychiatric hospitals, and from the self-report of addicted individuals, we know that there are some symptoms of alcoholism surrounding the patterns of drinking which are characteristic of the addicted individual. This is true of all alcoholics within the United States regardless of age.

The general characteristics of alcoholics are: preoccupation with alcohol, increased tolerance to alcohol, gulping drinks, drinking alone, using alcohol as a medicine, blackouts, protecting the supply, and unpremeditated drinking. An individual is considered to be an alcoholic when four or more of the above characteristics exist. While there is some dispute as to an exact definition of each of these symptoms, they are usually described in the following manner.

The alcoholic is usually preoccupied with the next time he will be able to drink. He thinks about drinking at inappropriate times and at times when he should be concerned about other matters. Preoccupation with the experience of "getting high" is the indication of any kind of drug dependency.

Research has substantiated that increased tolerance to alcohol is characteristic of the young alcoholic. Such an individual can drink up to five times as much as a social drinker, and in the first hours of drinking this individual will report stimulating rather than sedative effects of the drug. The reason for this difference in reaction to alcohol is unknown but has been reported frequently.

As with other drug dependencies a person takes the drug for its effect and, therefore, will attempt to acquire as much as possible in the shortest possible time. Gulping drinks is characteristic of an alcoholic individual. He usually orders a double Martini, double Manhattan, a double shot, etc., because his primary intention in drinking is to "get high." This is the goal of any drug dependent person and the experience he becomes "hooked on."

Drinking alone is not diagnostic in itself, but most social drinkers drink merely to be social. Sociability is not an important factor in addictive drinking, and an alcoholic will drink at home when no one else is drinking. He will stop in a bar and drink by himself and will otherwise drink in situations where the only possible pleasure is the alcohol itself.

Once an alcoholic recognizes the exceptionally rewarding effects of alcohol, he often thinks of alcohol as a sort of panacea. He will use it as a medicine and especially as a tranquilizer for tension, anxiety, or sedation. Most alcoholics will think of alcohol when they are suffering from any form of disagreeable symptom or psychological stress.

Blackouts are a form of amnesia. On the morning after a heavy drinking bout the alcoholic has difficulty recalling some of the events of the previous evening. He may wake up and not be able to recall when he returned home or may not be able to remember some of the later events of the previous evening.

Sometimes the alcoholic feels more comfort-

*Veterans Hospital, Minneapolis, Minnesota.

able if he knows that alcohol is available. He feels reassured when he knows that there is sufficient alcohol at home, in the trunk of his car, in his office, or in his desk, in the event that he may need a drink sometime. Preoccupation with having a sufficient supply on hand is a trait of any drug dependency.

The alcoholic drinks more than he planned or knows he should drink. His drinking is often different than he would like it to be. As an example he may lose control on one or more occasions; he may stop for one or two drinks on the way home and end up intoxicated. Anyone who responds positively to the question: "Is your drinking any different than you would like it to be?" is probably suffering from alcoholism.

As mentioned before, if a person has four or more of the above eight symptoms, there is no question that he is an alcoholic because he has affected a predominately non-social use of alcohol, the end of which is to "get high" and, consequently, an obvious manifestation of psychic dependency on alcohol. Once a person has a drinking pattern as listed above he will not be able to successfully alter or change this pattern no matter how or what he tries. His only recourse is total abstinence, for if he continues to drink the consequences he will encounter physically, psychologically, socially, maritally, economically, and vocationally are definitely predictable. The pattern of drinking described above is acquired by the alcoholic through experimentation with alcohol whereby he achieves the optimum desired response. Because there is no definite standard of normal drinking in our society and, consequently, no education as to what is an alcoholic type of use, the alcoholic simply does not know that his drinking is abnormal or different from others. The physician alerted to these eight symptoms and signs can help the alcoholic by recognizing his chemical dependence. It follows that once his chemical dependence is recognized, the appropriate treatment measures can be instituted. Since the estimated number of alcoholics range as high as one in ten males and one in fifty females who drink, it is sufficient to note that medical management cannot possibly be instituted in all of these individuals.

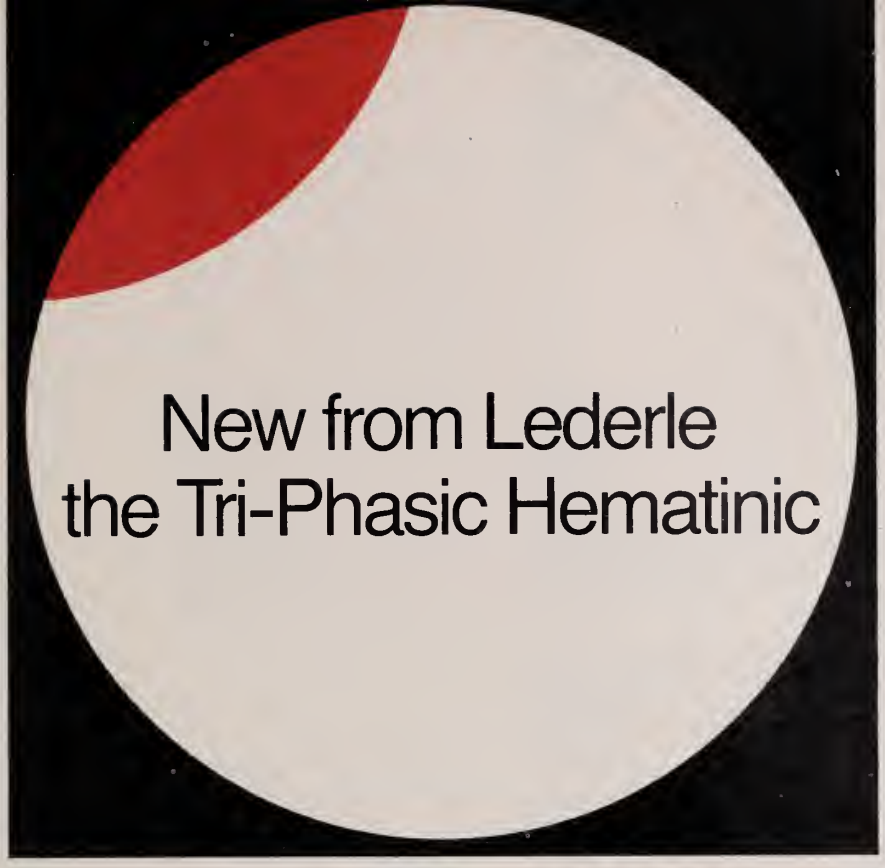
Group therapy through Alcoholics Anonymous, specialized alcohol treatment programs in general hospitals, and specialized treatment centers outside of general hospitals are increasingly being used as resources in the community. These have been successful because they focus on the addiction and what to do about it rather than analyzing its cause.

The biggest danger physicians face in treating alcoholics is in prescribing ataractics or tranquilizers which are potentially habit forming. Librium*, Equanil*, Valium*, Serax*, the barbiturates, and other drugs are potentially habit forming and should not be prescribed for alcoholics. Some of these agents are useful in the withdrawal phase of the seriously-addicted individual but certainly should not be used on a maintenance basis. Alcoholics, and other kinds of drug dependent people, are notorious switchers in the sense that they can switch from alcohol to a minor tranquilizer or barbiturate with great ease. Incidentally, once an individual begins using a habit forming drug other than alcohol, he usually begins drinking after a short period of time.

Conclusions

There are some early signs and symptoms the physician can look for as a guideline in diagnosing the syndrome of alcoholism. This is a true drug dependency that falls within the scope of most medical practices. Early diagnosis and referral of the addicted individual are necessary for a successful outcome. There are treatment resources in almost every community in the United States which are interested in helping the addicted individual. All physicians should use extreme care when prescribing drugs to chemical-dependent persons, especially alcoholics. The alcoholic can switch from alcohol to one of the substitutes with relative ease. The inclination of alcoholics to "swallow something" to solve their problems can be carried from the "golden glass" to the medicine cabinet and it behooves all of us to make certain that we do no harm to our patients.

LIBRIUM	brand name for CHLORDIAZEPOXIDE
VALIUM	brand name for DIAZEPAM
EQUANIL	brand name for MEPROBAMATE
SERAX	brand name for OXAZEPAM



Specifically formulated with
vitamins and minerals important
in the treatment of anemia



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421-1

Fracture Conference

Comminuted Fractures of the Femur*

MARK B. COVENTRY, M.D.,† PETER L. BOMAN, M.D.† and
EINER W. JOHNSON, JR., M.D.†

Dr. Peter L. Boman:

Our first case is that of a 77-year-old real estate agent who was in a head-on automobile collision two weeks prior to his admission at the Mayo Clinic. The driver of the other car was killed and his wife suffered a fracture of the fifth lumbar vertebra and severe abdominal contusions from her lap seat belt. The patient was initially treated in another hospital for a midshaft comminuted fracture of the left femur, a comminuted fracture of the left tibia and fibula, fractures of both bones of the contralateral forearm, and concussion and multiple facial lacerations. He also suffered two broken ribs.

After he had been treated for shock and the lacerations had been sutured, the forearm was placed in a padded, wooden splint with a pin placed through the tibia for traction. The roentgenograms made on admission here are shown in Figure 1.

*Fracture Conference, April 8, 1968.
†From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.



Fig. 1—(Case 1). Anteroposterior (*Left*) and lateral (*Right*) views of left femur and upper tibia two weeks after injury, showing comminuted fractures of distal femur and proximal tibia.

Dr. Mark B. Coventry:

The patient was an elderly man, and we were worried about his general condition—shock, pneumonia, fat embolism—but he survived all these. His local physician had put a pin in the tibia and applied a Thomas splint. Since the time of injury we had been in touch with the local physician, who had taken excellent care of the patient and then transferred him to our service for definitive orthopedic care. The main objective is to get a functioning lower extremity, so that he can walk. How are we going to do this, Doctor Irwin?

Dr. Jack C. Irwin, Jr.:

If he were younger it might be easier to gain union by plating the lower end of the femur. As far as the tibia is concerned, I do not think one could help that much by internal fixation. I believe one should try to mold the fracture into the best possible position and then attempt to hold it by applying a cast or using traction. Traction would have the advantage of letting him move the knee. With a cast, it would probably be difficult to regain motion. For comminuted fractures, traction is probably the best method.

Dr. Coventry:

There seem to be about six fragments present. What else is available other than traction? Would you wish to open this fracture?

Dr. Irwin: That would be difficult.

Dr. Coventry:

Yes, I agree, and most difficult to rearrange and hold with any type of internal fixation. Are any other methods available?

Dr. Irwin:

You could place the extremity in a cast. One would have to reduce it under general anesthesia; but this would probably not be a good method of treatment since it would be difficult to maintain the reduction in a cast because of the degree of comminution.

Dr. Coventry:

Some shortening would probably occur. You eliminated the use of intramedullary rods, Dr. Irwin. Why?

Dr. Irwin:

The fracture is too low and too comminuted to be treated that way effectively.

Dr. Coventry:

Now, as to the tibia on the ipsilateral side, we have a pin there, well placed by the local physician, and we will not disturb it. This aligns the tibial fracture well and should be good definitive treatment. Are you concerned about the posterior bowing of the femur at the fracture site?

Dr. Irwin: Yes.

Dr. Coventry: How will we correct this?

Dr. Irwin:

You can put a folded towel under it. I would put him in a Thomas splint with a Pearson attachment to allow for flexion of the knee.

Dr. Coventry:

Correct. You would put a towel under the fracture site. Anything else? Are we going to pull this femur down with the pin below the tibial fracture? What if we should get some distraction of the tibial fragment while doing this?

Dr. Irwin: This would certainly defeat both purposes.

Dr. Coventry: How would you remedy it?

Dr. Irwin: It would probably be easier to remedy by putting a pin through the distal femur.

Dr. Coventry:

This is what we did (Figure 2). The single pin placed previously is pulling through a fractured tibia and then through the knee, and this traction is expected to transmit force to the very strong muscles of the thigh. But that is impossible. So we put a Kirschner wire through the distal fragment of the femur and put the pull on it. We also retained the pin in the tibia with only three or four pounds of weight on it. The pin in the distal femur not only maintained length and lateral alignment there but also corrected the posterior bowing by pulling anteriorly as well as distally. Do you think the bowing is overcorrected?



Fig. 2—(Case 1). Anteroposterior and lateral views of left femur after Kirschner wire had been placed through distal femur two and a half weeks after injury.

Dr. Irwin: It is a little overcorrected.

Dr. Coventry:

A little bit. So we can lessen the traction a few pounds. We are talking about alignment, and alignment means overall restoration of the contour of the femur, considering both joints involved and the natural configuration of the bone. Displacement is not alignment. We have good alignment here but also displacement of about half of the shaft in the lateral position. We do not care about this because we want only union with good alignment. We also desire restoration of length, and we have established that.

The patient was in traction for six weeks and, when he showed good callus formation roentgenographically, we put him in a spica cast (Figure 3).



Fig. 3—(Case 1). Anteroposterior and lateral views of left femur 10 weeks after injury, in spica cast.

Dr. Boman:

Initially, when we took him out of the spica cast, he had bony union but rather limited knee motion of about 25° to 30° but after a little exercise it had increased to 90° of flexion.

Dr. Coventry:

I think he is going to come along fine with the method of treatment we elected here. I am sure there are other ways of handling these fractures, but we preferred this rather conservative method. Union and a functional limb have been obtained.

Case 2

Dr. Boman:

The next case is similar. A 47-year-old man was working on a truck, straddling the saddle tanks on the side, when a car on a grease ramp rolled down and struck his left lower extremity, severely crushing it. He was taken to his local hospital where he was found to be in shock. Blood transfusion was given and he was then sent to this clinic. There was a large laceration in the popliteal area, marked swelling of the entire extremity, and fractures as shown (Figure 4).

Dr. Coventry:

These fractures are compounded and again there are fractures of the femur, tibia, and fibula of the same extremity. There is also a large, gaping wound in the popliteal fossa. We saw him within a few hours of his injury. Dr. Beckenbaugh, what do we do first?

Dr. Robert D. Beckenbaugh:

The initial treatment has to be debridement of the compound fracture,



Fig. 4—(Case 2). *Left* and *Center,* Anteroposterior and lateral views of distal left femur, showing distal fracture at time of injury. *Right,* Lateral view of left tibia and fibula at time of injury.

leaving the wound open. The tibial fracture is compounded only in the popliteal area. Is that right?

Dr. Coventry:

Yes, except for a one-cm hole with a spicule of the tibia sticking through it at the fracture site anteriorly. Thus it is minimally compounded from within. We must be sure of his vascular and neural status. His dorsalis pedis pulse was normal, but he had no peroneal nerve function. The back of the knee joint was wide open; we could look in and see the menisci. There were fractures of the tibial spines; one could put one's hand down into the calf to mid leg and up into the thigh halfway to the hip. But the popliteal artery and vein were uninjured. We did an extensive debridement, put in some drains, packed gauze loosely over the wound, and then turned our attention to the fractures. There are problems here. How would you proceed?

Dr. Beckenbaugh:

Initially, I would do nothing in the way of internal fixation of the fractures. But I agree with open packing of the wound in the popliteal area and debriding the compound fracture. I would anticipate that he would be placed in a Robert Jones type dressing, with some arrangements made for changing the pack, for two or three days before an attempt at closure of the popliteal wound and internal fixation of the tibial fractures.

Dr. Coventry:

He was fortunate in having this wound posteriorly, so it drained dependently as he lay on his back in bed. Nature was working for him. We saw no reason not to go right ahead and put in Kirschner wires for traction and place the extremity in a splint. The initial injury had created a right angle flap and we had to extend it rather widely for exposure to debride the wound. When we finished we put in some loose sutures to hold this flap over the blood vessels and so cover them.

There now is a pin through the distal fragment of the femur, and a localizer is used to control angulation laterally. How are we going to get some traction on the tibia?

Dr. Beckenbaugh:

If you think the alignment is not good enough you can put in a calcaneal wire, place the leg in a cast, and apply traction.

Dr. Coventry:

We did just as you suggested—put a pin through his os calcis; then the extremity was put in a Thomas splint with a Pearson attachment, and he was started on antibiotic therapy. After three days, we dressed the wound, took out the drains and packs, and finished up our closure using irrigation-suction tubes.

Dr. Boman:

The roentgenograms at 32 days after injury (Figure 5) show good progress; alignment is good and callus is visible.



Fig. 5—(Case 2). At 32 days after injury. *Left* and *Center*, Left distal femur. *Right*, Left tibia and fibula.

Dr. Richard S. Bryan:

There is another method for dealing with the same type of thing: utilizing a cast, attaching the pins with plaster, and using a modified Russell strap, leaving the entire posterior part open with the two pins acting as a sling.

Dr. Coventry:

During World War II, when we had so many of these injuries due to gunshot and shell-fragment wounds, we inserted pins, pulled the fractures out, aligned the limb, and put the extremity in a spica cast.

Case 3

Dr. Boman:

Our third patient suffered a fracture of the right midfemur in an automobile accident in 1929, when she was 19 years of age. Her initial treatment at that time had been a bone graft and insertion of a six-hole plate. Within a few months she had no evidence of healing and was brought here for definitive treatment. In August 1929 the plate was removed and some straightening done for the bowing of the femur.

Dr. Coventry: Was an osteotomy done?

Dr. Boman:

No, she had non-union, and the femur was manipulated back into straight alignment. In September 1929, when there was no evidence of healing, tibial grafts were inserted at the fracture site, after which good union was attained. The patient got along well until 1949, when she began to have pain in the right knee, especially on the medial aspect. This became progressively worse,

and she came here in 1956 for evaluation. There was degenerative joint disease in the right knee, especially on the medial side. By 1966 she had severe pain with activity; she had motion in her knee from 25° to 80° (Figure 6).



Fig. 6—(Case 3). Anteroposterior and lateral views of right knee 38 years after fracture of right midfemur.

Dr. Coventry:

This is 37 years after fracture. The alignment in the anteroposterior direction looks good, but there is some lateral bow (varus), as a result of which she has put abnormal stress on her knee for the last 37 years. The alignment we have been talking about this morning should be preserved at all costs because, as the years pass, malalignment produces abnormal loading stresses which may produce degenerative changes in the adjacent joints. This patient surely represents such an example.

Dr. Boman:

In April 1966, Dr. Coventry explored her knee, removed the medial meniscus, and found several loose bodies in the joint, which were removed. Then he did an upper tibial osteotomy (Figure 7). The patient did well postoperatively and by December 1966 had no pain with motion, an almost normal gait, and a range of motion from 0° to 60°. She is walking essentially pain-free, with a good gait.

Dr. Coventry:

We used the anterior approach here and retracted the patellar tendon to the right when we were doing the left side and to the left when we were doing the right side. We used two staples for fixation of the osteotomy. We went anteriorly because we wanted to take a large anterior wedge to correct the flexion deformity and convert her 60° of motion to a more useful arc. We knew we could not increase it, however. She can now put her foot down with her knee straight instead of bent at 30°. Her varus deformity is also corrected.

Dr. Emanuel Semerad:

Why do you think the medial joint had narrowed originally when her initial fracture healed with lateral bowing?



Fig. 7—(Case 3). At eight months after upper tibial osteotomy.

Dr. Coventry:

When there is lateral bowing, one gets more stress on the medial tibial and femoral condyles due to varus. If there is medial bowing, one gets valgus of the knee. With lateral bowing, as this patient has, one gets bowleg deformity; and bowleg opens the lateral compartment but loads the medial.

Dr. Boman:

On reviewing the literature, one finds many forms of treatment for multiple fractures of one extremity including intramedullary rod, plates and screws, skeletal traction, and immobilization in plaster. When one considers fractures in the distal third of the femur, one has to remember the muscle groups that come into play: the quadriceps, the adductors, the hamstrings, and the gastrocnemius. In intercondylar and supracondylar fractures the gastrocnemius muscle may produce joint incongruity by causing posterior angulation or displacement of the fracture, or by rotating and spreading the condylar fragments.

The quadriceps and hamstrings produce longitudinal forces which produce overriding and angulation of the fragments or driving of the proximal femoral fragment into the suprapatellar pouch, causing further displacement and hemorrhage.

Valgus deformity, which is frequently seen, can be caused by the strong pull of the adductor magnus and longus. Fortunately, vascular and neurologic damage in these fractures is rare but must always be watched for.

Stewart and co-workers' reviewed the experience at the Campbell Clinic with fractures of the distal third of the femur. Two hundred thirteen patients were followed for more than a year. The fractures were divided into two groups according to method of treatment: closed methods and open methods. Closed methods included skeletal traction using one or two pins, casts, simple splinting, and skin traction. An excellent or good result was defined as 130° of flexion of the knee without much pain on motion and walking without a limp. The patient with a poor result had moderate or severe pain, 90° or less flexion, and moderate or severe limp. The results of the closed methods

are shown in Table 1. Skeletal traction was used chiefly in 84 cases. The results of open treatment methods are shown in Table 2. Blade plates, Rush pins, Knowles pins and screws, intramedullary nailing, and intramedullary bone graft were used for fixation. Their biggest series was with Knowles pins and screws. Overall, results were good or excellent in 67% of cases treated by closed methods and in 54% treated by open methods.

TABLE 1
Results of Closed Treatment*

Method	Cases	Results	
		Excellent or good	Fair or poor
Skeletal			
One pin	50	33	17
Two pins	34	27	7
Casts	54	32	22
Splint	4	3	1
Skin traction	2	2	0
Total	144	97	47

*Data from Stewart and co-workers.[1]

TABLE 2
Results of Open Treatment*

Method	Cases	Results	
		Excellent or good	Fair or poor
Blade plate	12	5	7
Rush pins	8	4	4
Knowles pins	40	24	16
Intermedullary nail	7	2	5
Intramedullary bone graft	2	2	0
Total	69	37	32

*Data from Stewart and co-workers.[1]

Anderson[2] reported results of closed treatment, in both children and adults, using Russell traction. His results for adults were similar to Stewart and co-workers.[1] His article emphasized more the care of children, in which the results generally were very good, as one would expect. The technique for pin traction is relatively easy. Actually, the femoral pin does not have to be inserted immediately. It can be done 24 to 48 hours later when one sees what degree of angulation will occur. At times the periosteum and the soft tissues will maintain alignment without this pin. Figure 8 shows a patient in this type of two-pin traction.

Dr. Coventry:

Dr. Boman has well summarized the various methods of treatment for fractures of the distal femur. We have presented two cases complicated by fibiale fractures as well on the same side. In my experience, balanced traction in a Thomas splint with a Pearson attachment has worked well. The two-pin technique is surely worthy, because it gives control of the distal fragment and will overcome its tendency to flex posteriorly.



Fig. 9—Example of two-pin traction.

Careful alignment should be striven for; degenerative joint changes in the knee (or hip or ankle) may develop if bowing of the femur occurs.

References

1. Stewart, M. J., Sisk, T. D., and Wallace, S. L., Jr.: Fractures of the Distal Third of the Femur: A Comparison of Methods of Treatment. J Bone Joint Surg [Amer] 48:784, 1966.
2. Anderson, R. L.: Conservative Treatment of Fractures of the Femur. J Bone Joint Surg [Amer] 49:1371, 1967.

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Organization

AMA Membership

DESPITE STATEMENTS to the contrary by some segments of the press and certain politicians, the AMA continues to represent the majority of American physicians. At this time when the practice of medicine is facing perhaps its greatest challenges, it is vital that a strong, effective national organization be sustained.

Hopefully, every Minnesota physician will be stimulated by this brief article to give thoughtful introspection to the importance of national representation through his AMA membership.

The purpose of the AMA is "to promote the science and art of medicine and the betterment of public health."

It offers help to physicians in keeping up to date on every phase of modern medicine and serves the public in a thousand unseen ways each day.

The story of the AMA is a story of more than a century of medical progress in this nation . . . for since its founding in 1847, there has been no major public health program in the United States in which the AMA has not played a significant role. To recount all of the accomplishments and discuss all the current activities, programs and services the AMA is engaged in would require several volumes of this journal, so the following resume of AMA activities should be viewed as merely examples of how the AMA serves medicine and the nation, and how it serves you.

AMA's Organization

The AMA is a democratically organized federation of 54 states, commonwealths and territorial medical associations. These, in turn, are composed of more than 1900 component county medical societies. The representative government principle applies throughout, with authority moving up from the component societies through the state societies to the national body through the process of elected delegates. As a member of the AMA, you have a voice with your vote if you choose to exercise it in electing state delegates and thereby determining the Association's leadership and policy.

From the office at 535 N. Dearborn Street in Chicago, the AMA maintains 80 Councils and Committees. The AMA staff and nearly 1000 volunteer physicians, working without remuneration, carry out the work of the organization.

Major Areas of AMA Activities

Scientific Meetings

The AMA sponsors more than 1000 meetings a year. Its Annual and Clinical Conventions, held each June and November, are the most important postgraduate medical study sessions in the world. Postgraduate programs encompass some 400 scientific lectures under the auspices of 23 specialty sections of the AMA. The AMA has sponsored meetings, and long offered leadership in such areas as occupational health, cost and distribution of care and the fight against pollution.

Accreditation

The AMA represents physicians in the accreditation of medical schools, postgraduate education and continuing education programs. It represents the needs of physicians in the accreditation of hospitals and establishing essentials for training allied health personnel.

Ethics

One of the paramount reasons for founding the AMA was to develop an accepted code of ethical conduct for physicians. Through the Judicial Council, the AMA continues to exercise responsibility as the developer, repository and arbiter of medical ethics.

AMA Library

The Archives Library of the AMA receives in an average month over 3000 research requests from physicians and others, and 750 requests for brochures. They have over 4500 films available and send out approximately 25,000 pages of photocopied material each month.

AMA Publications

Publications are a highly important part of the Association's program. The AMA is one of the world's largest publishers and about 12 million dollars of the budget goes into paper, printing and mailing.

* *The American Medical News* has a circulation of 20 million newspaper per year.
* The AMA has available approximately 1300 different pamphlets on child care, health education, sex education, diet and nutrition,

smoking, first aid. etc.

* The AMA has mailed free over 5 million pamphlets on the "Pill."
* *Today's Health,* a consumer magazine, is published monthly by the AMA.
* 100,000 kits on drug abuse have been sent to medical societies and individual physicians.
* *JAMA*, The Journal of the American Medical Association, is the most widely circulated medical journal in the world.
* To meet the needs of the specialties, AMA publishes 10 monthly specialty journals.

These and numerous other books and publications have been asked for by the physicians of this country, the public, the schools of this nation, allied health professions, health institutions, government agencies, and the more than 1900 state and county medical societies. As a result AMA researches, designs, publishes and prints these tens of millions of pieces every year. This is the responsibility of the AMA to the physicians and to the people of this country and one which will continue to be fulfilled only by a strong membership.

AMA Law Division

One of the most active divisions of the AMA is the Law Division which supplies to all departments, the Board of Trustees and physicians throughout the country, legal opinions and guidance, information on medical liability, taxation, insurance, advertising, copyrights, etc. Tens of thousands of physicians write every year and receive guidance on these and other problems.

AMA-ERF Programs

The American Medical Association Education and Research Foundation (AMA-ERF) established in 1962 has arranged over 46 million dollars in loans to more than 19,000 medical students, interns and residents in direct contributions. The AMA has received and distributed over 35 million dollars to medical schools in this country.

AMA Department of Investigation

The Department of Investigation has one of the largest collections of nostrum and quack gadgets and medications. It maintains the largest files in existence on health quackery and wages a relentless battle against cultists and charlatans throughout the country every year.

Health Care Delivery

The AMA has sponsored many programs to provide leadership and examples in the field of health care for the poor and in field of rural health care. Among them are inner-city health centers, donations of two mobile health units to a Chicago slum area . . . financing of health care projects by the Student AMA . . . and encouragement of innovations in methods of taking care of patients in areas of need and sparse physician population.

Legislation

The AMA through its Washington office and Council on Legislation reviewed over 1500 separate bills pertaining to medicine during the past session of Congress. In the last year, the AMA appeared before Congress in support of such measures as funding for medical school expansion, increased financial aid to medical students, appropriations for hospitals and medical facilities expansion, drug abuse education, vaccination assistance programs and numerous other positive proposals. The AMA's own proposal for financial health care—Medicredit—has received wide Congressional support as it is fiscally sound and would assure availability of health care for all without endangering traditional physician-patient relationships. It is also sponsoring legislation to create Peer Review and Utilization Review systems to operate through state medical associations.

Important Congressional appearances were also related to such subjects as HMO's, National Health Insurance Bills, the National Cancer Program and many others.

This affirmative legislative stance has been well received in the present Congress as many members of the Senate and House from both sides of the aisle will attest.

In addition, AMA's representatives meet frequently with representatives of the various administrative and regulatory agencies in Washington. Proposed regulations are closely reviewed and appropriate testimony is offered.

AMA Membership and Finances

There are approximately 345,000 physicians in this country including those not actively engaged in the practice of medicine (there are 198,000 office based physicians). Current AMA membership is 205,000. Approximately 46% of the total AMA budget is derived from physician dues, the remainder, about 54% comes from advertising

and exhibit revenues. Your AMA dues of $110 would have to be about $250 were all the operational costs of the AMA to be financed by membership dollars. Further, it should be noted that of the 1972 budget over 80% will be expended for educational and scientific programs designed to improve the quality of American medicine.

Conclusions

While we have discussed in this paper only a representative sample of the many current activities of the AMA, it should be apparent even to the casual reader, that the physicians of Minnesota need a major national organization to represent them. I believe that physicians want and need a strong effective organization which will carry forward positive programs whose beneficial effects will be realized by all the people in this country.

Medicine today is facing strong forces attempting to direct restructuring of the health delivery and health financing systems with increased controls on physicians and patients alike.

In the next few years, this nation will finally decide whether the patient may choose the physician he will see and whether the physician will provide treatment in accordance with the patient's medical need or in accordance to budgetary or administrative decisions.

The physician body needs a strong representative group more than at any time in history to represent us in these crucial times. Every physician should ask himself this question: "Who would represent him and carry out all the aforementioned activities if there was no AMA?" I submit there is no other organization now able to carry out all of these functions.

It is mandatory that there should always be constructive reassessment of the AMA, but it must be realized there will never be complete agreement on all issues. Minnesota has maintained through the years a high level of AMA membership, but we need more house officers and students to broaden our base of representation.

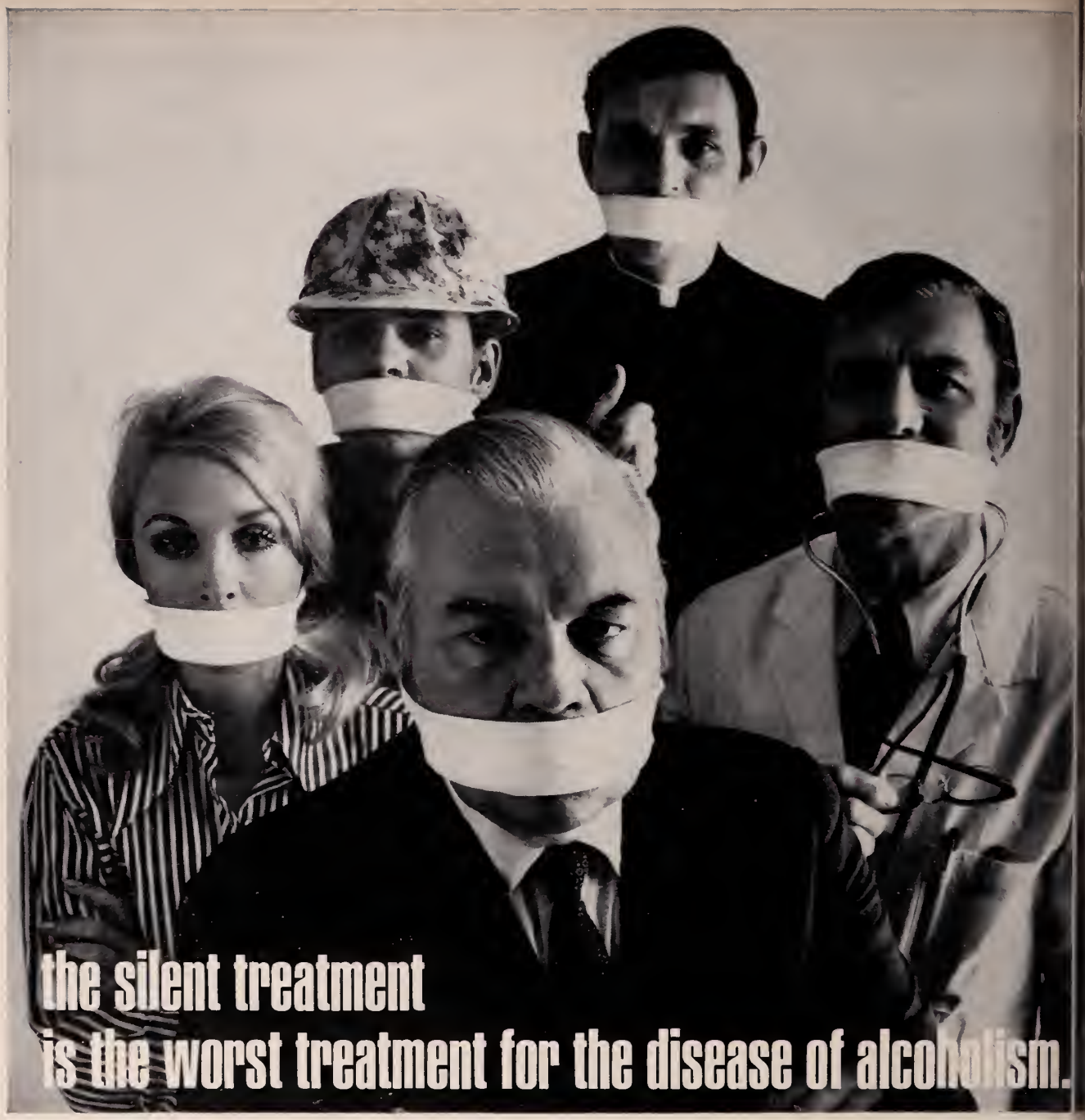
If you feel the AMA does not represent you, or does not stand for its espoused purposes, "to promote the science and art of medicine and the betterment of public health," you can quietly drop your membership and lose your voice for effective action; or you can complain to others "that blankety blank AMA has goofed again." Your local society and the Minnesota State Medical Association would much rather hear of your opinions and your dissatisfaction. How else can your AMA delegate represent you?

I emphasize it is the responsibility of every physician to voice his opinions and become involved constructively to maintain a strong effective AMA.

George B. Martin, M.D.
AMA Delegate and
President-Elect
Minnesota State Medical Association

Reminder

119th Annual Meeting of the Minnesota State Medical Association in Rochester, Minnesota, May 18, 19 and 20, 1972.



When one out of 20 employees in America—including executives—has alcoholism, it's time for some plain talk about alcoholism. The alcoholic's family, friends and employer may mean well, but the silent treatment is no way to treat a disease. And alcoholism is a disease from which recovery is possible, rather than a moral weakness for which the alcoholic should be pitied—or fired. It's a disease which ranks with heart disease, cancer and severe mental disorders as a public health menace.

The National Council on Alcoholism has pioneered in setting up joint union-management alcoholism programs. In these programs, industry is achieving *recovery rates averaging 60 to 70 percent.* Management profits by retaining its experienced employees and regaining lost productivity—estimated at six billion dollars. Unions profit by increasing health and welfare protection for members and keeping them in the active work force.

If you think alcoholism is affecting your business, **talk it over with the Director of Labor Management Services, National Council on Alcoholism, 2 Park Avenue, New York N.Y. 10016.**

National Council on Alcoholism, Inc.



Book Reviews

THE FUNCTION OF THE MEDICAL OR DENTAL WITNESS IN A PERSONAL INJURY CASE by Robert C. Onan, Jr.

This is a paperback, mimeographed manual dealing with the problems of testimony by the physician or dentist as a witness for either the plaintiff or the defense. It provides a few sample physician's reports which could serve as a guide for the physician who is confronted with the need for providing such a report.

Carl O. Rice, M.D.
Minneapolis, Minnesota

SYNOPSIS OF CLINICAL CANCER, 2nd EDITION by Condict Moore; Publisher: C. V. Mosby Co., St. Louis; Price: $11.75; Pages: About 265; Illustrations: 22.

This book comprises an interesting synopsis on about 25 different organ cancers. The material is well chosen for a basic orientation about cancers in general and for the young clinician it is an excellent point of departure for the study of the most commonly encountered carcinomas.

In each instance it deals basically with the incidence, etiology, pathology, natural history, diagnosis and principles of treatment, deliberately leaving the more extensive and specific details to other sources.

Bibliographic references are adequate and largely current. With the chapter headings and the excellent style of editing, the index proves to be adequate.

Carl O. Rice, M.D.
Minneapolis, Minnesota

THE RIGHT TO TREATMENT by Donald S. Burris; Springer Publishing Co., Inc., New York

This is a symposium by about thirteen different authors dealing principally with medical-legal problems: principally those of the socially, economically, and financially underprivileged individuals in relation to their right to treatment in a society that has constantly striven for improvement but has not yet attained perfection. It presents a series of interesting and provocative socio-economic and humanistic problems. Well worth reading!

Carl O. Rice, M.D.
Minneapolis, Minnesota

TUBERCULOSIS by J. Arthur Myers; Warren H. Green, Inc., St. Louis, Missouri; Pages: 353, Price: $8.50.

This well-prepared book is a review of the medical lifetime of one man, beginning at age four, when he had his first awareness of consumption that took the lives of so many people in the years preceding the turn of the century and for a number of years thereafter.

Dr. Myers became progressively more interested in the numerous facets of tuberculosis and has continued to devote his life and energy to the care of, and the eventual conquest of, pulmonary tuberculosis.

The book is a history of the epidemiology of tuberculosis. It gives the experiences of a man and the numerous ramifications of his studies and ever increasing knowledge. He traveled a million miles in this country and abroad, teaching, writing and lecturing on tuberculosis. Without J. Arthur Myers the conquest of tuberculosis could not have attained the success that is now evident in our generation.

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Minneapolis, Minnesota

HOUSE OF A THOUSAND BABIES by Frances W. King-Salmon, M.D.; Pages: 169; Price: $5.00; Exposition Press, New York.

This well written book represents the experiences of an American woman physician in China between the years 1922 and 1940. The young, affable, enthusiastic Frances W. King was one of the co-founders of the Woman's Christian Medical College in Shanghai. Dr. King-Salmon's experiences were thrilling, unique, sometimes horrifying, but always humanized because of her profound interest in people and the society of human beings. Through the Sino-Japanese War in 1937 she saw the collapse of the Chinese dollar. She pointed out the progressively decreasing buying power of a hundred dollar CNC bill, which in 1937 would buy two cows, but which in 1947, under the influence of the rapid takeover of communism would buy only one-third of a pack of matches.

This book should be read by every American because of its sheer fascination. It should be read by all physicians because it has been written from the eyes and the mind of an intellectual physician, and it should be read by all people who have concern for our country, lest we too, in the rat race that we are pursuing, fall victims to an irreversible inflation that no one can afford and without a haven for any one of us to return to.

Dr. Frances W. King-Salmon has portrayed a lifetime of experience that could, in a generation or two, be our own—unless we take heed.

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Minneapolis, Minnesota

MEDICAL PHYSIOLOGY, by William F. Ganong; Pages: 573; Lange Medical Publications, Los Altos, California 1971.

This is a well constructed paperback volume, covering every practical phase of medical physiology. It is comprised of eight sections which include the major divisions of human physiology within which are incorporated 40 chapters, each dealing with a specific function.

The abbreviations and symbols, which are commonly used in physiology, are defined in the Appendix. The alphabet system, which is being used progressively more often in medical literature, calls for the need of a Medical Abbreviations Dictionary, which in this instance is thoughtfully supplied in the Appendix and without which an uninitiated physician runs into the conundrum of translating the numerous and often unnecessary alphabet abbreviations.

This valuable book is wholeheartedly recommended for every physician who is in the practice of modern medicine.

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LINICAL RESPONSE	"T_3 and T_4 ratio veries eccording to glend source. Fluctuations in response can occur. Potency cen vary."[3]	"Sodium levothyroxine has been extensively used with satisfaction end is widely held to be superior to (desiccated) thyroid."[7] "There ere well documented exemples of petients who felled to respond satisfactorily to desicceted thyroid but subsequently responded to (sodium-1) thyroxine."[4]
REDICTABILITY	Failure of thyroid U.S.P. treated patients to show clinical improvement and/or lack of correlation in clinical findings to thyroid function test results has been frequently discussed in the literature.[8,9,10,11,12,13,14,15,16] Regardless of which fector or fectors accounts for this phenomenon the fect remains thet discrepancies do occur.	Test results predictebly eleveted. ". . . orel potency of this materiel is attested to by e uniformly good clinical response corroboreted by e prompt end sustained increese in the serum PBI levels."[16]

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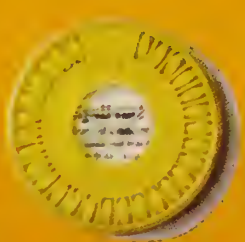
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Unscored 5 mcg.	N.A.	N.A.	unscored ¼ gr.	¼ gr.	0.025 mg.
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25 mcg.	1	1	unscored 1 gr.	1 gr.	0.1 mg.
N.A.	N.A.	N.A.	N.A.	1½ gr.	0.15 mg.
50 mcg.	2	2	unscored 2 gr.	2 gr.	0.2 mg.
N.A.	3	3	unscored 3 gr.	3 gr.	0.3 mg.
N.A.	N.A.	N.A.	unscored 5 gr.	5 gr.	0.5 mg.
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Precautions: As with other thyroid preparations, an overdosage may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Disease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

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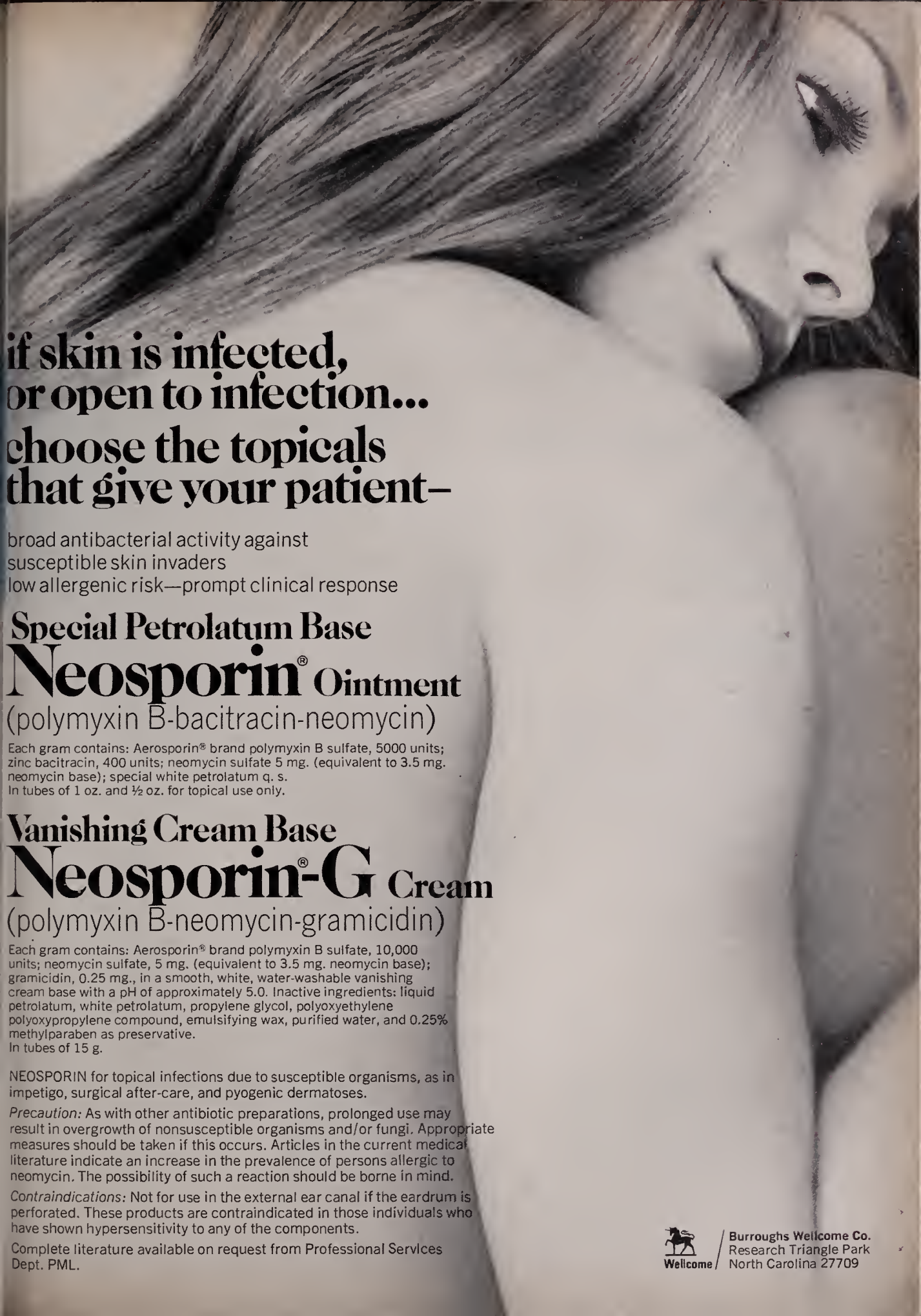
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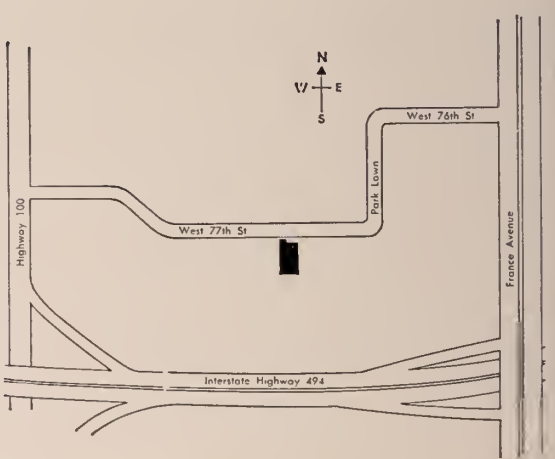
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Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type peins can be the presenting symptom of leukemia.

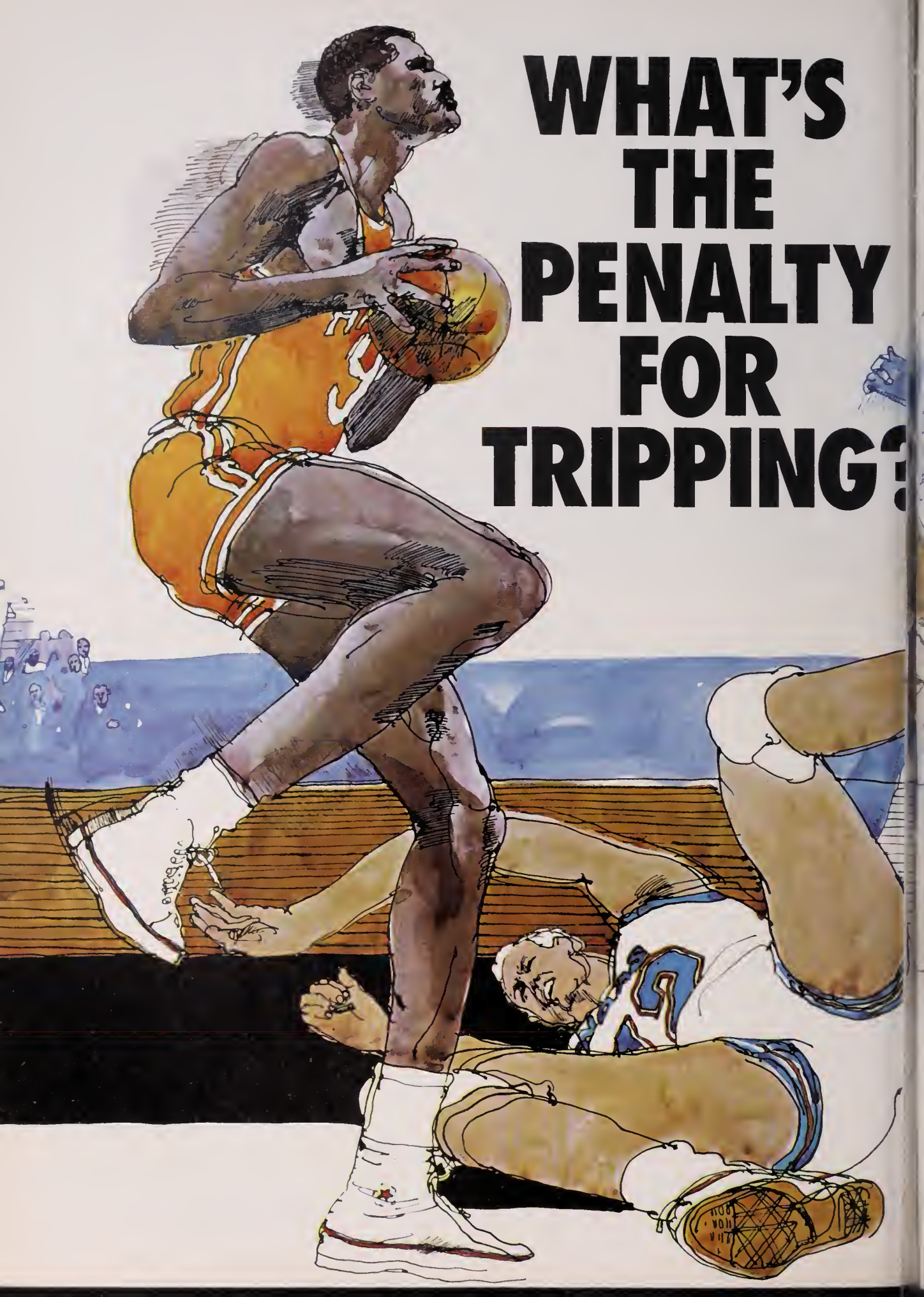
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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., certain elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**--they can both cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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President's Letter

Annual Meeting

MANY CHANGES are being made to make our Annual Meeting of the Minnesota State Medical Association more attractive to the members. The dates for our meeting are May 18, 19 and 20, and it will take place on Thursday, Friday and Saturday, with Saturday A.M. being reserved for our specialty societies. We hope that in the future, many of our specialty societies will be able to hold their annual meetings in conjunction with the State Association Annual Meeting.

By holding the Annual Meeting at the end of the week, we hope that many busy physicians will find this more convenient, and we are not competing with the opening weekend of fishing season. I am sure that many of our physician-fishermen will be pleased to know that they can open the fishing season properly and also attend our annual meeting.

The Committee on Scientific Assembly has done a terrific job in providing an interesting program with an excellent group of speakers. I want to thank Doctor John Mayne, Chairman of this Committee, for doing such an efficient job. The variety of program subjects is unsurpassed. The speakers will make brief, informative presentations. No presentation will be more than 15 or 20 minutes. This enables more subjects to be covered. With the variety of subjects being presented, I can assure that all physicians in Minnesota will find topics in their special interests. The afternoons of Thursday and Friday will be devoted to panel discussions of general subjects.

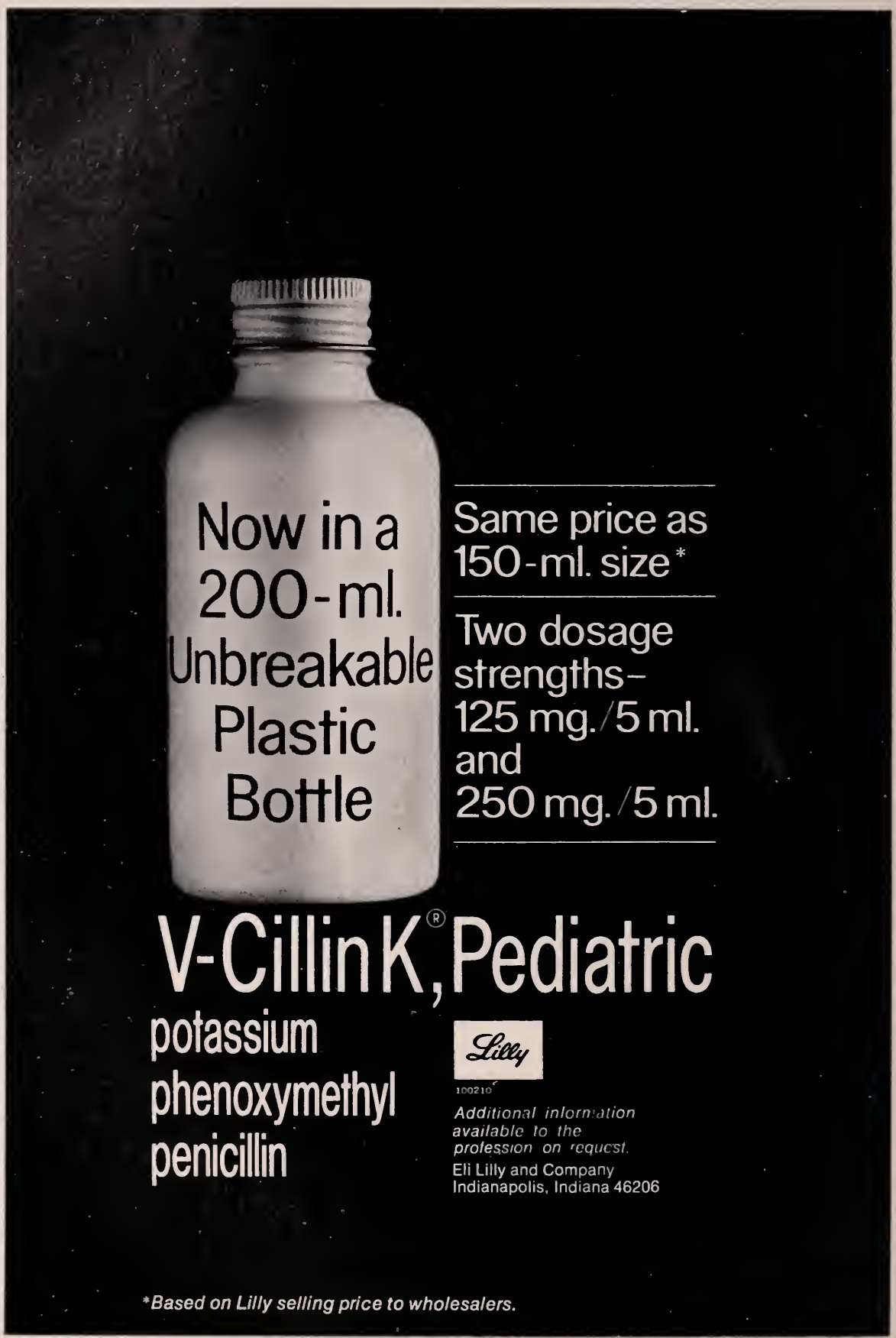
I would like to take this opportunity to invite all members of the Minnesota State Medical Association and their wives to attend the President's Reception at 6 P.M. on Thursday evening and the Annual Banquet at 7:00 P.M. Donna and I would like to meet as many of you as possible. There will be excellent entertainment during the banquet and dancing to follow the banquet. The Women's Auxiliary has also planned an active program so there will be a great deal of activity for the physician's wife.

The Annual Meeting is the most important function of our Minnesota State Medical Association. Good attendance is a symbol of the strength of the Association.

With these many changes that are being initiated, I hope that every one of our members and their wives will want to attend the Annual Meeting of the Minnesota State Medical Association.

Robert T. Kelly

President
Minnesota State Medical Association


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The Arthritic Hip*

Current Concepts of Surgical Management

DAVID S. BRADFORD, M.D.†

RECONSTRUCTIVE SURGERY of the hip has undergone great advances in the past decade. Improvement in techniques and prosthetic implants has furnished a means of reconstructing arthritic hips previously felt unsalvageable. The family physician has assumed an increasingly important role in the management of patients with painful hip disease. It is desirable, therefore, that he have an adequate understanding of operative indications and treatment. This manuscript is presented as a review of the pathology of degenerative and rheumatoid arthritis involving the hip, the clinical manifestations, and the current concepts of surgical management.

Pathology[14,18,19]

The intelligent planning and execution of surgery is dependent on recognition of the pathology initiating the arthritic process. By far the most common type of arthritis affecting the hip joint is osteoarthritis or degenerative arthritis. The pathology is characterized by cartilage fibrillation, osteophytes, and subchondral bone formation. Microscopically, the cartilage will demonstrate surface irregularities with fissures running parallel to the collagen fibers. Chondrocytes may be clumped at the base of the fissures suggesting attempts at repair. Special stains will show a loss in metachromasia secondary to a decrease in acidic glycosaminoglycans. X-ray examination of the hip may show narrowing of the joint space secondary to the loss of surface cartilage. Similarly cyst formation and sclerosis immediately below the joint surface and osteophytes at the margin of the cartilage or at points of ligament and capsular attachments may be identified. Primary osteoarthritis occurs de novo without known predisposing factors. Secondary osteoarthritis develops from alternations in the normal joint structure slipped epiphysis, hip dysplasia, (Perthes' disease), in association with metabolic disease (ochronosis, spondyloepiphyseal dysphasia, acromegaly), or following trauma, infection, or avascular neucrosis.

Rheumatoid arthritis on the other hand begins basically as an inflammation of the synovium. The pathologic synovial tissue, although non-specific histologically, demonstrates edema, congestion, fibrin exudation, and cellular infiltration. As the synovium becomes thickened it is thrown into folds or villi, spreading over the cartilage surface as a pannus eroding the cartilage as well as subchondral bone. Periarticular tissues may likewise become involved. This may lead to contractures of capsule, ligaments and muscle groups. X-ray changes consist of periarticular swelling, joint space narrowing, generalized demineralization and bony erosion.

Clinical Features[18]

Pain is the most frequent complaint in patients with an arthritic hip. Pain arising from osteoarthritis develops insidously. Initially it is intermittent and relieved by rest and mild analgesics. The pain is located over the trochanter, or groin, or referred to the knee, and is aggravated by movement. Often patients may complain of night or rest pain. In primary osteoarthritis, patients rarely become symptomatic before 40-50 years of age. One-third may have bilateral hip disease.

In rheumatoid arthritis the features are less characteristic. Single joint involvement is rare. The disease process is noted for remissions and exacerbations, and great variation in areas of involvement and rate of progression are common. Fatigue, malaise weight loss, and early morning stiffness would be expected.

In both processes, hip motion is limited. The earliest findings would be loss of internal rotation and extension. Thigh atrophy is usual. An antalgic as well as a positive Trendelenburg gait likewise

*Presented in part at Continuation Medical Course in Basis of Care and Treatment of Arthritis—March 11-12, 1971, University of Minnesota, Office of Postgraduate Medical Education Health Science Center, Minneapolis, Minnesota.

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is frequent.

Indications for Surgery

Surgery for the patient with an arthritic hip is indicated to relieve pain, to correct and prevent deformity, and to maintain and regain mobility. The enthusiasm for new surgical techniques must not obscure the benefits of conservative treatment. In the patient with an arthritic hip, weight reduction, muscle strengthening exercises, analgesics, and the use of a cane are helpful. The use of a cane in the opposite hand of the involved hip is an effective method of reducing the load on the hip joint.[29] A push on the cane will produce a moment in the same direction as that produced by contraction of the abductors on the contralateral side. As Blount has noted,[8,9] the static force normally present on a hip of 85 pounds can be reduced to 66 pounds by a downward push on the cane of 38 pounds. Finally the management of the total patient rather than a single arthritic joint must be stressed. In the rheumatoid arthritic patient with a painful hip, proper medical evaluation and treatment should be well under way before considering reconstructive surgery.

Types of Operations

Synovectomy and Soft Tissue Procedures

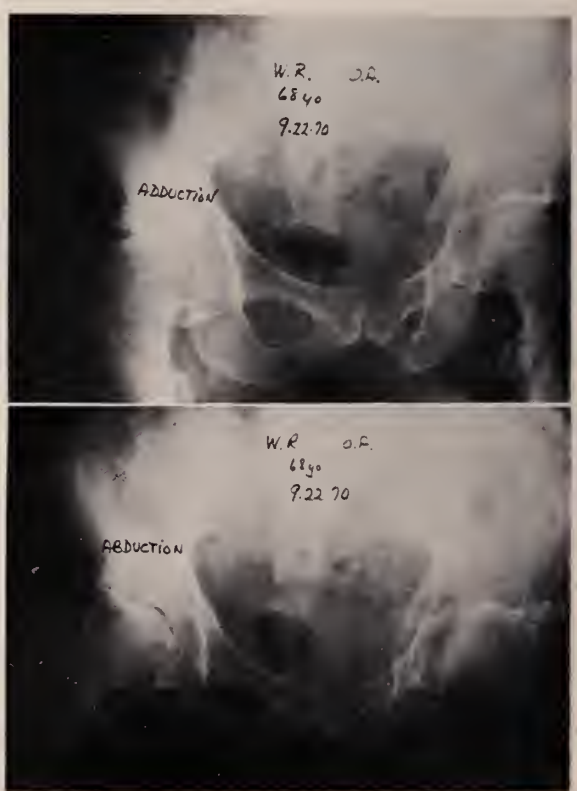
Early synovectomy, particularly in the juvenile arthritic patient, might be considered for the ease of persistent, painful synovitis, unresponsive to medical management. Experience with this procedure is not widespread, although Albright[1] has recently presented a limited series that suggest further trials are indicated. There is little evidence to suggest that surgical dislocation of the hip to facilitate the synovectomy has lead to avascular necrosis of the femoral head. Soft tissue procedures, consisting of muscle releases, tenotomies, capsulotomy, and neurectomy, have proven of some benefit in relieving hip pain in the osteoarthritic patient.[23,27] Their effect for the most part is usually shortlived. These operations are of greatest benefit when combined with more definitive procedures.

Hip Fusion[20,33]

Hip fusion is an effective and predictable method for the treatment of degenerative arthritis of the hip joint. It may be indicated when the arthritis is confined to one hip, destruction of the hip is marked, motion is limited, and pain is severe. It finds more use in the younger individual whose work would require heavy labor. Successful arthrodesis can be expected to produce a stable, pain-free hip. In rheumatoid arthritis, with multiple joint involvement, and usually bilateral hip disease, arthrodesis of a single hip is not justified.

Osteotomy[9,14,19,28]

The principle of osteotomy is one of realigning the joint relationship to that resting or weight bearing position that improves or maximally restores the joint space radiographically. It is presumed that the radiographic appearance of a widened joint space denotes a regeneration of joint cartilage. The operation may entail an abduction, displacement, or rotation repositioning (Figure 1-4). The optimal position of the osteotomy is in the inter—or subtrochanteric area. Recent evidence suggests that the benefits of osteotomy might involve circulatory and biochemical alterations in bone and cartilage[30] as well as biomechanical factors brought about by change in head-shaft relationship.



Figures 1 (top) and 2—Xrays of the right hip in a 68-year-old male patient with severe painful osteoarthritis demonstrating an apparent improvement in the joint space width to a greater degree in abduction.

The indication for this procedure would involve significant and disabling arthritic hip pain in a patient that has at least 60 degrees of hip flexion. Following surgery, pain relief and improved ability to ambulate are to be expected. There is little change in the amount of hip motion, although cyst formation and sclerosis are reversed. The use of compression fixation techniques facilitates healing of the osteotomy and allows early ambulation. Partial weight bearing with crutch support is necessary for several months until bony union is solid.

Osteotomy has proven a poor procedure in the management of rheumatoid hip disease. The basic pathology is not altered by this procedure and consequently symptoms are not relieved.

Excisional or Resection Arthroplasty

Resection of the femoral head and neck is rarely indicated as a primary procedure for arthritis of the hip. Its value for the most part rests as a salvage operation for treating sepsis developing after mold arthroplasty or other reconstructive procedures. It will produce a moveable, relatively pain-free hip, but the patient will need external support because of gait instability and limb shortening (Figure 5-6).

Femoral Head Replacement[7,10,17,24,32]

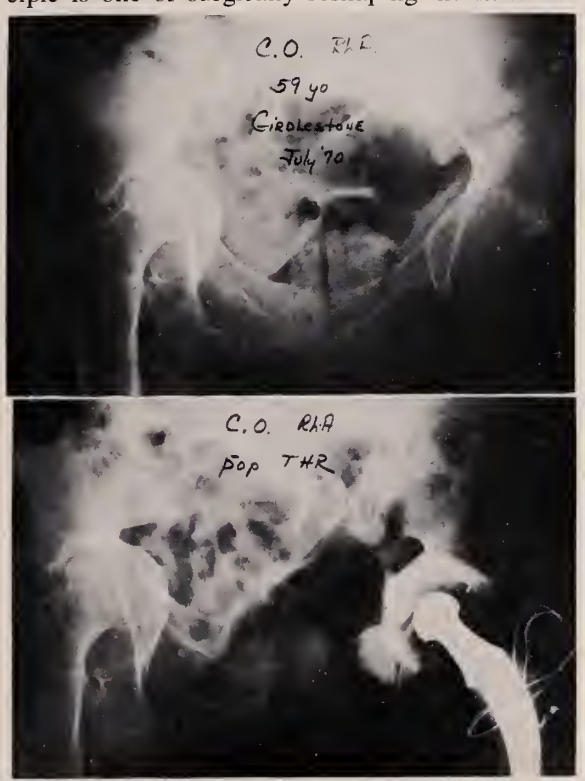
Femoral head replacement arthroplasty for the management of the rheumatoid hip is a poor procedure. The bone in rheumatoid arthritis is usually quite osteoporotic and cannot be expected to support a metallic implant. Pain developing from prosthetic loosening and migration of the femoral head into and through the acetabulum occurs frequently (Figure 7-8). In the younger individual with degenerative arthritis secondary to aseptic necrosis, femoral head replacement might be the preferred method providing the acetabulum is relatively uninvolved by the arthritic process.

Interpositional Arthroplasty[3,4,5,7,21,24,32]

Interpositional, mold or cup arthroplasty remains a valuable procedure in the treatment of arthritis of the hip joint (Figure 9-10). The principle is one of surgically reshaping the head and



Figures 3 (top) and 4—The plan for an adduction osteotomy is outlined preoperatively. The approximate wedge of bone to be removed in order to assure an abducted position of the head in relation to the shaft is marked. The osteotomy is then securely held by a compression plate. The clinical result to date has been gratifying.



Figures 5 (top) and 6—Xrays demonstrate a Girdlestone resection of the left hip performed in a rheumatoid arthritic patient because of severe pain and limitation of motion. Following surgery the pain persisted and ambulation was difficult because of instability. Total hip replacement has furnished a stable, pain free, mobile hip.

acetabulum, interposing a metallic cup, followed by relief from weight bearing for a period of several months to allow fibrocartilage to form over the acetabulum and femoral head. In the younger rheumatoid patient with unilateral hip disease and little involvement of other joints, and in the active individual with degenerative arthritis, it is a useful procedure. The requirements of rehabilitation are great, and limited weight bearing with crutch support for four to six months is desirable. Pain relief, increased mobility, and improved gait can be expected in the majority of patients if properly selected. Results from bilateral cup arthroplastics in rheumatoid patients are less satisfactory and revision of the cup by secondary procedures because of limitation of motion is often necessary.

Complications of cup arthroplasty are similar to any type of hip surgery. One possible advantage, however, is the possibility of salvaging a cup after sepsis.[22] This is usually impossible after other methods of implant surgery and the implant in those cases must be removed.





Figures 7 (top) and 8—An Austin-Moore prosthetic replacement in a 57-year-old rheumatoid arthritic patient has resulted in prosthetic migration through the acetabulum. Total hip reconstruction with firm fixation of the components with methylmethacrylate (outlined in the dotted areas) has salvaged a difficult problem.

Total Hip Replacement[11,12,15,25,26,31,34]

The recent advent of total hip replacement pioneered by Charnley, McKee-Farrar, and Ring, have revolutionized the othopedic approach to the arthritic hip. The principle is replacement of the femoral, as well as the acetabular surface with an inert material of satisfactory design, firmly fixed to the bone with a plastic cement, methylmethacrylate. A rigid bond between bone and implant is essential and serves to distribute the stresses over the broad area providing a gradual transition of stress between prosthesis and bone. The present available models consist of either a metal to high density polyethylene or a metal to metal joint.

Generally, total hip replacement arthroplasty would be favored for the severe, symptomatic degenerative hip in a patient older than age 55. Patients with severe rheumatoid arthritis involving multiple joints, and patients with failed, painful prosthesis, might be considered for this type of surgery at a younger age.





Figures 9 (top) and 10—Mold arthroplasty has furnished this rheumatoid arthritic patient with a pain free and mobile left hip. Periarticular ossification and medial migration of the cup has not compromised the result to date.

The results for this type of operation are predictably excellent. Most authors report greater than 90% of the patients are completely or almost completely relieved of all pain, and a similar percentage of patients will notice a greatly increased range of motion and an improved ability to ambulate. In the rheumatoid arthritic patient the ability to walk great distances may not be increased because of the multiple joint involvement, but this group of patients will ambulate in a limited area with greater agility and freedom from pain. Long-term results are not available. From the experience of others, which is now approaching eight years, it appears that tissue reaction to the methylmethacrylate is not objectionable. With the use of a plastic acetabulum socket, a minimal projected wear had been estimated as 25 years.[12] Replacement of the acetabulum component is possible. However the long-term effects from debris accumulation around the joint from socket wear is not known.

It would appear that this procedure, properly executed, can produce superior results that are unmatched in consistency by other methods. Until long-term results are known, however, restraint in the use of this technique particularly in younger individuals, is desirable.

Complications

Complications following hip surgery would include thromboembolic problems, infection, periarticular ossification, nonunion of osteotomies and prosthetic dislocation, or loosening. Thromboembolic disease occurs frequently following hip surgery and prophylactic anticoagulation has been advocated.[16] Sepsis developing after hip surgery can usually be managed satisfactorily with closed suction irrigation techniques.[13] Sepsis following total hip replacement, however, is a major catastrophy. Salvage is rarely possible short of removing all the components and cement and converting the arthroplasty into a resection.[2] With meticulous attention to surgical technique, control of operating room traffic, and proper operating room air filtering systems, infection can be reduced to a level below 1%. The merits of laminar flow operating room facilities in reducing infection have not been firmly established. On the other hand, prophylactic antibiotics would appear to be valuable in limiting the incidence of this complication. Infection may not become manifest until as long as one or two years after surgery. Therefore, continued follow-up by the physician and surgeon is essential.

Summary

The indications, prognosis, and possible complications of reconstructive surgery for the arthritic hip have been outlined. Careful evaluation and assessment of each patient, along with thorough understanding of surgical principles and goals, is paramount to a successful operative result.

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22.-34. See page 324.

Vitreous Floaters and Flashing Lights

Vitreous Collapse and Sequelae

DENNIS M. ROBERTSON, M.D.*

UNDER ORDINARY CIRCUMSTANCES, one is not aware of the many imperfections in his own ocular media. With the exception of the aqueous humor, all of the ocular media are less than perfectly transparent, because they are composed of tissues containing cells with their nuclei. Opacities toward the front of the eye, involving the cornea and lens, even when of moderate size, frequently are not subjectively recognized as opacities, because the umbra of their shadows do not fall on the retina. In general, small opacities must be located within the vitreous cavity before they cast a shadow on the retina and are subjectively appreciated. Vitreous opacities are mobile (within limits) and, accordingly, are recognized by the patient as moving or floating spots; hence, the term "floaters." Spots, specks, or defects in the vision that appear stationary to the patient usually are not due to vitreous opacities. These stationary opacities, not the subject of this discussion, may indicate significant pathologic changes elsewhere than in the vitreous and merit investigation to determine their cause.

Most vitreous opacities (floaters) are entirely harmless, and the patient needs nothing more than reassurance. However, they may indicate serious ocular disease. The problem, then, is to establish which of them are significant.

Anatomy of Vitreous Cavity

Basically, the vitreous is a transparent gel in which there is suspended a solution of salts, plasma proteins, and hyaluronic acid. Its skeleton consists of a fine meshwork of interlacing collagenous fibrils. Its cellular makeup is confined to a few relatively large flat cells situated anteriorly within the superficial layers of the vitreous. Normal vitreous contains no blood vessels.[1]

From this information, one can appreciate, then, that floaters may arise from two sources: (1) from within the vitreous itself, because of alterations in its structure, most usually a collapse of the vitreous body, with condensation of collagen fibrils, and (2) from cells or debris invading the vitreous cavity from elsewhere: for example, clumps of leukocytes appearing in response to an inflammation, such as uveitis, or aggregates of erythrocytes and fibrin strands resulting from hemorrhage into the vitreous cavity.

Relationship of Vitreous Body to Retina

The vitreous body and the retina are intimately associated by virtue of a structure called the inner limiting membrane of the retina. This membrane is composed of both the cortical fibrils and mucoproteins of the vitreous and the plasma and basement membranes of the innermost cells of the retina (Muller cells and astrocytes). This vitreoretinal union, though delicate, is a definite

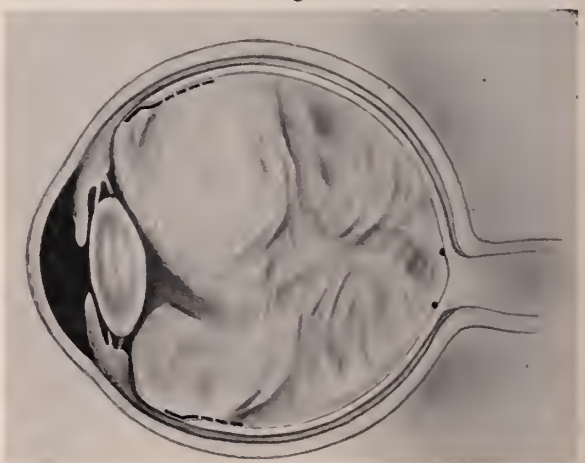


Fig. 1—Relationship of vitreous to other structures of eye. Normally firm vitreoretinal adhesions at region of ora serrata and also at optic nerve are indicated by solid lines anteriorly and black dots posteriorly. Interrupted line indicates posterior extension of relatively firm anterior vitreoretinal adhesion that occurs with aging and disease.

*Mayo Clinic and Mayo Foundation, Rochester, Minnesota.
See editorial, page 344.

one, but it is relatively firm only anteriorly near the ora serrata, and posteriorly in a small area about the optic nerve head (Figure 1). The union of the vitreous with the retina becomes less firm in its middle and posterior thirds after the second decade. Contrariwise, with increasing age or in the presence of inflammatory disease, the relatively firm anterior adhesion at the ora serrata generally extends further posteriorly[2] (Figure 1).

Changes in the Vitreous

Syneresis

Liquefaction, more properly called syneresis, and collapse of the vitreous with posterior separation of the vitreous from the retina occur naturally with aging and high myopia. These changes may also occur after trauma to the globe or in association with other pathologic conditions, such as uveitis. Posterior vitreoretinal relationships are such that, when syneresis and posterior vitreous collapse occur, interruption of the normally delicate union between the retina and the vitreous generally will not produce complications from traction on the retina. However, significant bleeding may occur if one of the superficial capillaries is torn because of excessive traction on the superficial retina when the vitreous detaches. Whether hemorrhage occurs or not, a ring-shaped vitreous opacity on the posterior face of the detached vitreous frequently can be seen with the ophthalmoscope (Figure 2). This ring represents condensed vitreous that formerly was attached to the peripapillary retina.

Anteriorly, where the vitreoretinal bond is relatively strong, vitreous collapse may cause traction on the retina sufficient to tear some of the superficial blood vessels in the retina and occasionally to produce full-thickness retinal tears (Figure 3). Because retinal tears are precursors to retinal detachments, such an occurrence is obviously serious.

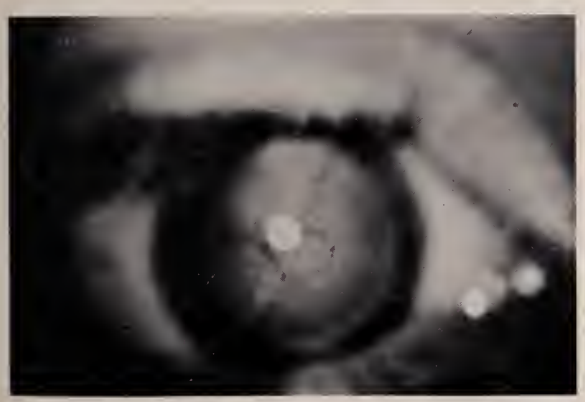


Fig. 2—Ophthalmoscopic view of ring-shaped vitreous opacity associated with posterior vitreous separation. This condensed vitreous ring formerly was attached at peripapillary retina.



Fig. 3—Superior vitreous collapse and retinal tear caused by traction of vitreoretinal adhesion.

Condensation of Vitreous Framework

Condensation of the vitreous framework to form entoptically visible floaters, though considered to be a normal phenomenon in the aged, also occurs in younger persons.[3] Generally, these vitreous changes are insidious and produce only subtle symptoms. Most persons with floaters have recognized them for years. They are usually described as specks or strings with occasional dot-like enlargements. Such floaters are usually not significant. However, floaters that appear suddenly and in great numbers are always significant. Acute floaters may appear as a web or lace-like mesh or simply as a shower of small opacities. Generally, these symptoms indicate a hemorrhage into the vitreous, a sudden collapse of the vitreous body, with or without hemorrhage, or an acute inflammatory reaction with cellular exudation into the vitreous. Possible complications resulting from vitreous collapse must be carefully investigated, and the cause of inflammation or bleeding must be established.

Hemorrhage

Hemorrhage into the vitreous may occur in a multiude of conditions. Perhaps one of the more common conditions is diabetes mellitus, in which some of the abnormal, new vascular channels may suddenly begin to bleed. Acute vitreous collapse is another common cause. Other causes of vitreous hemorrhage include hypertension, occlusion of the central retinal vein, blood dyscrasias, trauma, and others too numerous to mention.

Inflammation

Symptoms of floaters caused by aggregates of leukocytes may be no different from those that

accompany intravitreal hemorrhage. A posterior uveitis may occur abruptly from various complex causes. If a focal uveitis is threatening the macula, prompt treatment may be extremely important.

Other

Causes of vitreous opacities other than those mentioned include asteroid hyalitis (of little significance, usually unilateral and frequently not appreciated by the patient, though the relatively large snow-white opacities are easily recognized by the examiner), amyloidoses, and foreign bodies, including parasites. Tiny glittering opacities (probably in some instances cholesterol crystals), which settle rapidly, are characteristic of synchysis scintillans, but this is uncommonly seen and occurs primarily in eyes severely injured by disease or trauma.

Symptoms of Light Flashes with Floaters

If vitreous opacities appear suddenly and are accompanied by a subjective sensation of light flashes, one should suspect an acute vitreous collapse and possible sequelae. Usually, the flashes of light occur in the temporal periphery, appear abruptly and are gone in one or two seconds. They may recur many times during the day or intermittently over a period of several days. Light flashes are probably caused when the vitreoretinal union becomes interrupted and when the collapsed vitreous body "bumps" into the retina during eye movements. Such flashing lights by themselves are not uncommon. They are frequently observed by older persons, especially at night, and, in such instances, they usually are insignificant.

When flashes appear acutely and in association with the sudden appearance of floaters, it suggests that the vitreous body has suddenly collapsed and begun to separate from the retina. (These light sensations should not be confused with the scintillation scotoma seen by patients with migraine. The latter are a specific type of visual disturbance, which present bilaterally and symmetrically as a zigzag pattern of shimmering lights, occasionally colored but more often not, lasts 15 to 30 minutes, and frequently, but not always, precedes a typical migraine headache.)

Sequelae of Vitreous Collapse

Several studies have shown that 10 to 15% of all eyes with symptoms from an acute vitreous collapse have retinal tears of one variety or another[4-6] (Figure 4). About one third of the eyes with horseshoe tears accompanying such an acute symptomatic vitreous collapse develop retinal detachment.[7-9] With special techniques, an ophthalmologist usually can recognize these tears and institute treatment in an effort to prevent subsequent retinal detachment. If a detachment has developed, the patient usually will notice a shadow that most frequently ascends from the inferior visual field. Provided the detachment is recognized early, when it is confined to the periphery and spares the macula, it usually can be satisfactorily treated, with excellent visual results. However, when the detachment has extended posteriorly to involve the macula, visual results after retinal reattachment are often disappointing. Thus, early referral in such cases is essential, for the optimal time to initiate treatment is at the hole stage, before the retina has actually detached.

Summary

Vitreous floaters are a common occurrence in the general population. Most are related to aging changes in the vitreous, appear insidiously,



Fig. 4—Fundus drawing showing two types of retinal tears seen with acute vitreous collapse. Along 3 o'clock meridian, there is a horseshoe tear with a small amount of free blood along its posterior border. Below tear, a round hole with its operculum is present. Operculum represents a plug of retina which, by virtue of a strong vitreoretinal attachment, has been torn completely away from surrounding retina. Vitreous still exerts traction on flap of horseshoe tear.

and are of little significance. However, acute symptoms of vitreous floaters that present either as a web, lace-like opacity or as a shower of spots should be considered of serious importance until the cause is diagnosed. Possible causes include intravitreal hemorrhage, uveitis, or, especially when accompanied by flashes of light, acute vitreous collapse, with attendant complications including retinal tears. The sudden appearance of floaters is always significant, though not necessarily always serious. Unless etiologic factors are readily apparent, these patients should be referred to an ophthalmologist for further evaluation.

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IT'S THE LAW

Physician Not Liable for Failure to Diagnose Tumor

The patient was involved in an automobile accident with injuries to the neck and right shoulder. He was seen and treated for a whiplash injury of the neck. He was seen by a second physician in consultation four months later. The patient stated that at this time his condition was improving. The examination of his shoulder was normal. Xrays were not ordered. Four months later the patient returned with more difficulty with his shoulder. Xrays were made which revealed a giant-cell tumor at the head of the humerus.

The patient brought a malpractice action against the examining physicians contending he suffered damage because of the physician's alleged negligence in failing to diagnose and treat the tumor of the shoulder. The trial court decided in favor of the physician and the patient appealed. The appeal court ruled that the medical record indicated that the physicians had taken usual medical care and that no negligence or malpractice was involved.

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Ross v. Hatchette, 251 So. 2d 820 (La. Ct. of App., Aug. 20, 1971). The Citation, Vol. 24, No. 6, January 1, 1972.

*The young are prodigal of life from a superabundance of it; the old are tenacious on the same score, because they have little left, and cannot enjoy even what remains of it.**

*William Hazlitt's essay: The Feeling of Immortality in Youth.

Multiple Primary Malignancies

An Unusual Combination

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BILLROTH FIRST RECOGNIZED the occurrence of different primary malignant tumors in one patient in 1869.[1] He was also the first to set forth the criteria of definition of multiple primaries. He stated that each tumor must be histologically different, that each must arise in a different location and that each must produce its own metastases.[1]

Today the most widely accepted criteria of multiplicity are those defined by Warren and Gates[5] (1932) in a review of the literature on multiple cancers up to that time. Their criteria, which differ little from Billroth's, were as follows: (1) Each tumor must present a definite picture of malignancy; (2) Each tumor must be distinct; and (3) The probability of one being a metastasis of the other must be excluded.

Since that time, numerous papers have been written on the subject. Moertel (1964) estimated the number of multiple cancers reported to that time in excess of 12,000.[4] Mersheimer, and coworkers (1964) reported on 140,000 cancer patient records obtained from the Connecticut Cancer Case Registry.[3] They found a total of 4,461 patients with multiple primaries but only five percent of these patients had more than two primaries.

Although multiple primary malignancies are not a rare entity their appearance is an unusual phenomenon which raises the question of: (1) predisposition in a patient with a single malignancy towards development of a second tumor; and (2) multicentricity of origin in certain tissues. Several authors have attempted to answer these questions and there is uniform agreement that multicentric cancers—that is cancers confined to the same tissue—occur more frequently than chance alone would allow.[4,6] Such uniform agreement has not been reached regarding the occurrence of a second primary in different tissues or organs.

Watson reviewed his cases in 1953, and concluded that there was no constitutional predisposition to multiple cancers of different systems and that no immunity was conferred by a first cancer.[6]

The patient presented in this report is of interest because of the unusual combination of tumors with which he presented.

Case Report

A 74-year-old retired Veterans Administration Hospital employee was admitted to the Veterans Administration Hospital for evaluation of black tarry stools for 1.5 months and epigastric bloating of a year's duration. During the same period the patient noted increased constipation, fatigue and anorexia. Over the last several months he had noted a ten pound weight loss. The patient denied any nausea, vomiting, hematemesis or abdominal pain.

Past history revealed an episode of malaria in 1917. In 1955, he was hospitalized for fulguration of four rectal polyps at 3, 6, 13 and 14 cm which were benign on miscroscopic examination. Since then he was followed periodically in the proctology clinic without evidence of recurrent polyp formation. The patient was admitted in February, 1969 because of suprapubic pain, nocturia and hesitancy. Cystoscopy revealed a tumor on

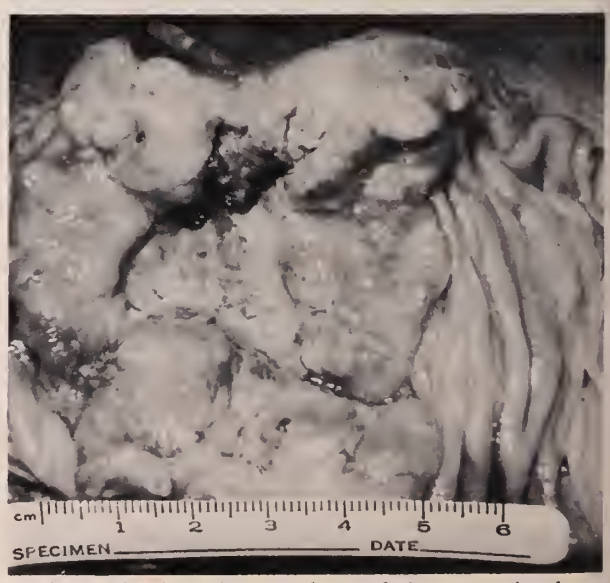


Fig. 1—Section of gross photo of the resected colon carcinoma.

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See editorial, page 341.

the left lateral wall of the bladder. A transuretheral resection (TUR) of the bladder tumor was carried out which revealed a transitional cell carcinoma grade I.

In April, 1969 he had a second TUR for obstruction secondary to benign prostatic hypertrophy.

In November, 1969, the patient was readmitted to the Urology Service for biopsy of suspicious lesion of the right lateral bladder wall. The lesion was a benign papilloma.

Physical examination on this admission revealed a well-nourished, well-developed elderly gentleman in no acute distress. His BP was 110/70 with a regular pulse of 80. Pertinent physical findings revealed external strabismus of the right eye with a 1 cm, soft, freely movable mass over the right lateral upper eyelid. The chest was found to be increased in the AP diameter with decreased breath sounds. There were no rales nor rhonchi present. There was a grade II/VI systolic murmur along the left sternal border. There was a tender 5 cm abdominal mass in the left upper quadrant near the midline. The abdomen was otherwise unremarkable. The remainder of the examination was within normal limits. Xray examination of the upper gastrointestinal tract revealed a transverse stomach with a small duodenal diverticulum but no other pathology was noted. A barium enema revealed an 8 cm constricting lesion of the upper part of the descending colon. A sigmoidoscopic exam was within normal limits to 20 cm.

Surgical Findings

The patient was taken to the operating room on April 22, 1970, with a preoperative diagnosis of carcinoma of the descending colon. Two separate tumor masses were identified at the time of surgery. One mass arose from the distal jejunum and had a marked inflammatory reaction in the surrounding mesentry with adherence of the involved loop to the mid-transverse colon. The other mass was located in the area of the splenic flexure and extended through the wall of the bowel to involve the anterior parietal peritoneum. There was enlargement of the regional lymph nodes but the liver and the rest of the abdomen were free of any gross evidence of tumor.

A left hemicolectomy and segmental small bowel resection were done. The patient did well following surgery and was discharged from the hospital 15 days later. He was given a course of chemotherapy (cytoxan) and is currently without evidence of any recurrence of disease.

Pathology

The specimen consisted of a segment of colon measuring 75 cm in length and an attached segment of small bowel measuring 25 cm in length.

There was an ulcerating tumor mass measuring 6 cm in length and encircling the colon 10 cm from the distal line of resection (Figure 1). Mi-



Fig. 2—Adenocarcinoma of the colon.

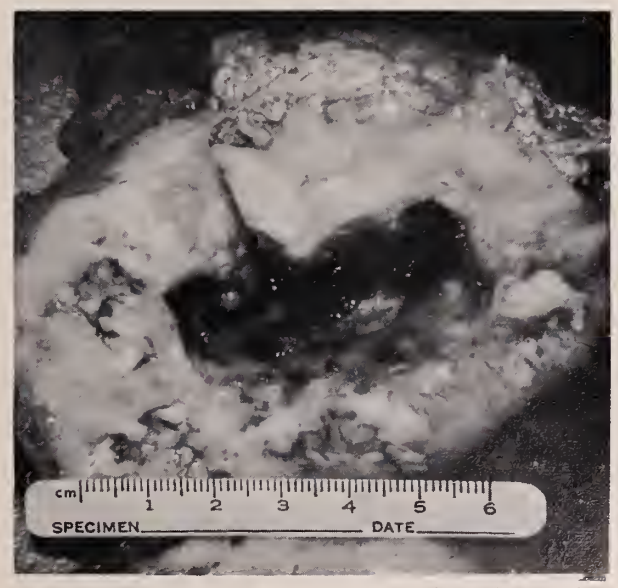


Fig. 3—Reticulum cell sarcoma of small bowel.

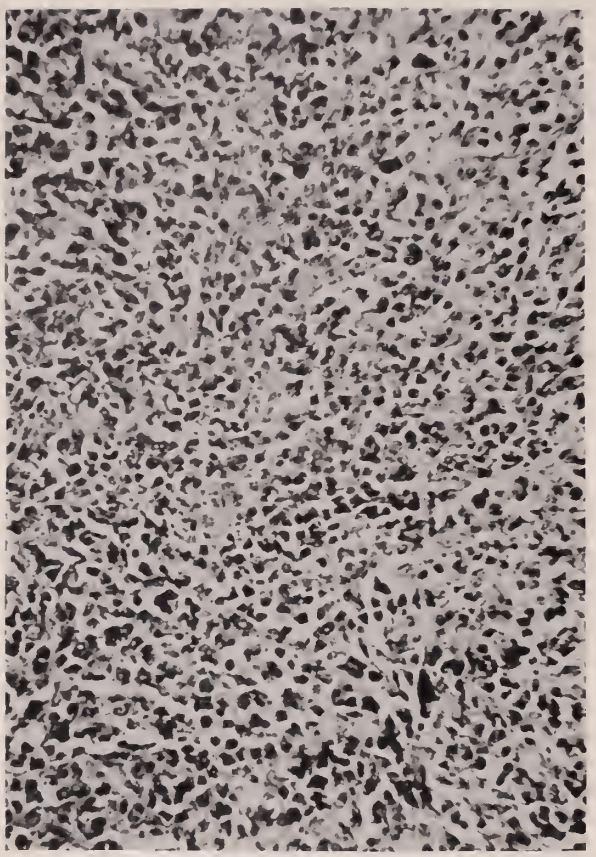


Fig. 4—Microscopic section of reticulum cell sarcoma of small bowel.



Fig. 5—Microscopic section of the reticulum cell sarcoma with reticular stain.

croscopic sections showed an infiltrating adenocarcinoma (Figure 2) extending through the bowel wall. Metastatic adenocarcinoma was present in one small adjacent lymph node.

Within the segment of small bowel was a large tumor mass measuring 9 cm in length and encircling the small bowel. There was extensive ulceration of the small bowel mucosa at the margins and the edges were raised and irregular. On transection the bowel wall measured from 2 to 3 cm in thickness and appeared to be completely replaced by soft pink-white tumor tissue with foci of necrosis (Figure 3).

Microscopic section showed the tumor to be composed of solid sheets of abnormal reticulum cells (Figure 4.). The tumor extended through the wall into the adjacent fatty areolar tissue. There were large areas of necrosis within the tumor. A reticulin stain showed numerous reticulin fibers between the individual tumor cells (Figure 5).

Lymph nodes taken from the portion of the bowel mesentery and omentum submitted with the specimen showed hyperplastic changes without evidence of tumor.

Conclusion

A case is reported of a patient with three different primary tumors believed to be the first with the following combination; 1) Transitional cell carcinoma of the bladder; 2) Reticulum cell sarcoma of the small bowel; and 3) Adenocarcinoma of the large bowel.

Multiple primary malignancies can and do occur concomitantly or, separated in time, in different tissues, in a significant number of patients presenting with apparent single organ disease.

The malignant stage of later appearing primary tumors is an index of the quality of follow-up care of the previously treated patient.

Surgery is a rational form of treatment in patients with multiple primary tumors. Each tumor should be approached with respect to its own biologic nature as well as to its effect on the patient as a whole.

See References 1-6 on page 332.

The Ruptured Disc Syndrome

EVAN S. ELLISON, M.D.*

BONY CONSTRUCTION of the spinal canal causes symptoms of nerve root pressure in the lumbar spine. Narrowing can be produced by a congenital anomaly, trauma or osteoarthritis. The stenosis may be present for a long time prior to the onset of symptoms. Further constriction of the canal by a bulging disc may initiate pain. In some cases the bony canal narrowing can be seen on the spinogram or standard views prior to surgery, but often the condition is not diagnosed until the time of operation.

Recent Studies

Schatzker and Pennal described narrowing of the spinal canal in the dorsoventral diameter or in the lateral recess with cauda aquina compression.[1] Jones and Thomson have attempted to assess spinal canal narrowing by measuring the A - P diameter of the canal and interpedicular distances in the prcoperative Xrays.[2] Macnab has documented nerve root kinking about the vertebral pedicle which can occur with narrowing of the disc space. He also described articular process impingement on the nerve root associated with disc space narrowing.[3] Schlesinger described first sacral nerve root pressure due to anatomical variation in the lateral bony recess.[4]

Symptoms

The symptoms of stenosis of the bony canal are similar to the classical symptoms of ruptured disc. The nerve root distribution of pain and numbness tends to be more constant and unrelieved by rest or a flexion brace. It is possible for the symptoms of spinal canal stenosis to have a sudden onset in a previously normal persons. The bony narrowing may have been present asymptomatically, but the slightest bulging of the disc will produce an acute onset of symptoms. The same amount of bulging in a normal spinal canal would be asymptomatic. There are no differentiating physical findings betwecn spinal canal stenosis and ruptured intervertebral disc.

Operation

At the time of the operation it is necessary to carry the laminectomy laterally far enough to visualize the lateral margin of the dura and nerve root without retracting either medially. This will allow direct visualization of any lateral, posterior or anterior bony canal narrowing. Sometimes the medial portion of the facet will have to be sacrificed. Before removing the overhanging bone it is often necessary to elevate it off of the constricted nerve root by means of the shoe of the Kerrison rongeur. As this is accomplished the indentation of the nerve root by the protruding



Fig. 1-A—Note lateral indentation of dye column at the L4-L5 interspace.

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Fig. 1-B—Note minimal indentation of dye column anteriorly indicating minimal disc protrusion.



Fig. 2-A—Note narrowing of bony canal by bony prominence adjacent facet.

bone becomes apparent. This phenomenon can also be caused by hypertrophy of the superior laminal plate posteriorly. It can also be found in scoliosis with lateral wall deformity. Osteoarthritic changes in the articular facets can produce this constriction by narrowing the lateral recess of the spinal canal at the point of exit of the nerve root or by indenting the dura medially. The spinal canal may be oval shaped with its largest diameter in the anteroposterior direction. This can in turn be associated with hypertrophy of the ligamentum flavum and facet and secondary pressure on the nerve roots laterally. The spinal canal may be narrowed in the anteroposterior plane and elongated laterally producing pressure on the nerve root anteriorly or posteriorly. The following three cases are examples of this condition.

Case Reports

Case 1

A thirty-six-year-old man had pain intermittently in the left buttock and left leg for six weeks. The pain was located over the posterior aspect of the left thigh and calf. The foot was not involved. He had backache on two occasions over the past six years but no previous radiation of pain into the legs. The present pain was aggravated by coughing as well as activity. Lying down relieved the pain. The pain was progressively worse.



Fig. 2-B—Note minimal indentation of dye column anteriorly.

Examination revealed loss of the normal lumbar curve. There was no motion of the lumbar spine on forward or side bending. There was spasm of the erector spinae muscles to palpation. The left calf measured 16 inches and the right 16½ inches in their greatest circumference. There was a positive straight leg raising test on the left at 30 degrees. The knee jerks and ankle jerks were equal and normal.

Xrays showed a large posterior defect in the dye column at the level of the 4-5 interspace on the left side (Figure 1). At surgery a hypertrophy of the superior laminal plate was found on the left side corresponding with the defect in the dye column. This was removed and the nerve root was completely decompressed. The patient was able to return to his former job two months after the operation with occasional mild twinges of pain in his left thigh which were receding.



Fig. 3-A—Note indentation of dye column by bony prominence adjacent facet.

Case 2

A forty-four-year-old man noted the onset of back pain while playing handball on March 7, 1969. The pain was located over the lateral aspect of the right buttock. It stopped at the thigh. There was numbness and tingling in all of his toes and in the sole of his right foot. Coughing did not affect the pain. Bending aggravated the pain. His past history revealed that he had scoliosis since childhood. Examination revealed spasm and splinting of the erector spinae muscles of the lumbosacral spine. There was scoliosis. There was no motion of the lumbar spine on forward or side bending. There was loss of the normal lumbar curve. The knee jerks were diminished bilaterally. The right calf measured 15¼ inches and the left 15¾ inches in their greatest circumference. There was a positive straight leg raising test on the right at 40 degrees. There was tenderness over the right sciatic notch.

Myelogram showed bilateral narrowing of the bony canal secondary to the scoliosis (Figure 2). At surgery



Fig. 3-B—Disc protrusion apparent on lateral view which compressed the nerve root against the bony prominence on the right side.

the bony narrowing of the canal was found as indicated on the myelogram. The narrowing indented the nerve root which was completely decompressed. The disc space was completely closed posteriorly and was not indenting the nerve. For this reason the disc was not removed. Six months after the operation the patient was playing handball and complained only of occasional twinges in the right thigh.

Case 3

A fifty-six-year-old man had pain in his back and right leg after unloading a truck three months prior to surgery. He had intermittent back pain for many years. The pain never radiated into the legs until the present attack when it extended down the posterolateral aspect of the right thigh into the right calf and into the lateral aspect of the right foot. It was constant, dull, and aggravated by activity. There was no paresthesia. Coughing aggravated the pain. There was also pain in his left buttock but much less than in the right. The patient obtained temporary relief wearing a William's brace but developed pain down the anterolateral aspect of the right thigh which was relieved by taking the brace off. Examination revealed spasm and splinting of the erector spinae muscles. There was no motion of the lumbar spine on forward or side bending. There was a list to the left side. There was loss of sharp sensation over the lateral apect of the left calf and left foot. Both calves measured 13½ inches in their greatest circumference. There was a positive straight leg raising test on the right at 30 degrees and on the left at 60 degrees. The toe extensors were normal.

The myelogram showed a large defect in the dye column which was confirmed at the time of the surgery (Figure 3). There was a large overhanging ridge of bone narrowing the lateral recess and compressing the nerve root on the right side. There was a bulging disc on the left side which was removed. Two months after surgery the patient complained only of minimal numbness in the lateral aspect of the right foot and some local aching in the incisional area.

The differentiation between ruptured disc and spinal canal stenosis is of interest to the diagnostician and to the surgeon. The direct cause of nerve root pressure is a bony constriction in the spinal canal aggravated by a protruding or ruptured disc. At the time of surgery the lateral margin of the bony canal has to be removed in order to determine that there is no constriction of the nerve root. Often in performing the dissection the lamina has to be carefully elevated off of the nerve before the overhanging bone can be removed. Adequate lateral dissection permits exposure for visualizing and removing the disc and complete decompression of the nerve root.

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Spontaneous Healing of Interventricular Septal Defects

Due to Nonpenetrating Trauma

BENJIE GOLDFARB, M.D.* and YANG WANG, M.D.*

RECENTLY, ROSENTHAL, Parisi, and Nadas reported the first instance of spontaneous healing of an interventricular septal defect due to nonpenetrating trauma that was documented by serial cardiac catheterization.[1] The case studied was that of a ten-year-old girl who was followed for a period of nine and one half years after a chest wall injury. Over this interval, there was a sizeable decrease in left to right shunt together with improvement in congestive failure. We recently have followed a similar case over a three and one half year period.

Case Report

A 20-year-old white male was well until November 1963 when he was involved in an automobile accident in which he fractured his sternum. He was hospitalized by his private physician and discharged after five days of observation. Two weeks later he was readmitted to the hospital in pulmonary edema. In adidtion, there was cardiomegaly, and a heart murmur was heard for the first time. He was treated with digitalis and bedrest, and on February 7, 1964 he was referred to the University of Minnesota Hospitals for further treatment.

Physical examination revealed a muscular, healthy appearing, white male. The blood pressure was 110/60. There were prominent "a" waves visible on examination of the cervical venous pulsations. A prominent right ventricular heave, a systolic thrill in the fourth intercostal space to the left of the sternum, and a palpable pulmonary valve closure were present on palpation of the precordium. On auscultation a grade IV/VI harsh, pansystolic murmur, loudest in the fourth intercostal space was heard along the left sternal border. The second sound was widely split with the pulmonic component being considerably louder than the aortic component. There was a loud apical protodiastolic gallop and a faint apical diastolic rumble.

A roentgenogram of the chest demonstrated probable biventricular enlargement with prominent pulmonary vasculature suggestive of a left to right shunt (Figure 1).

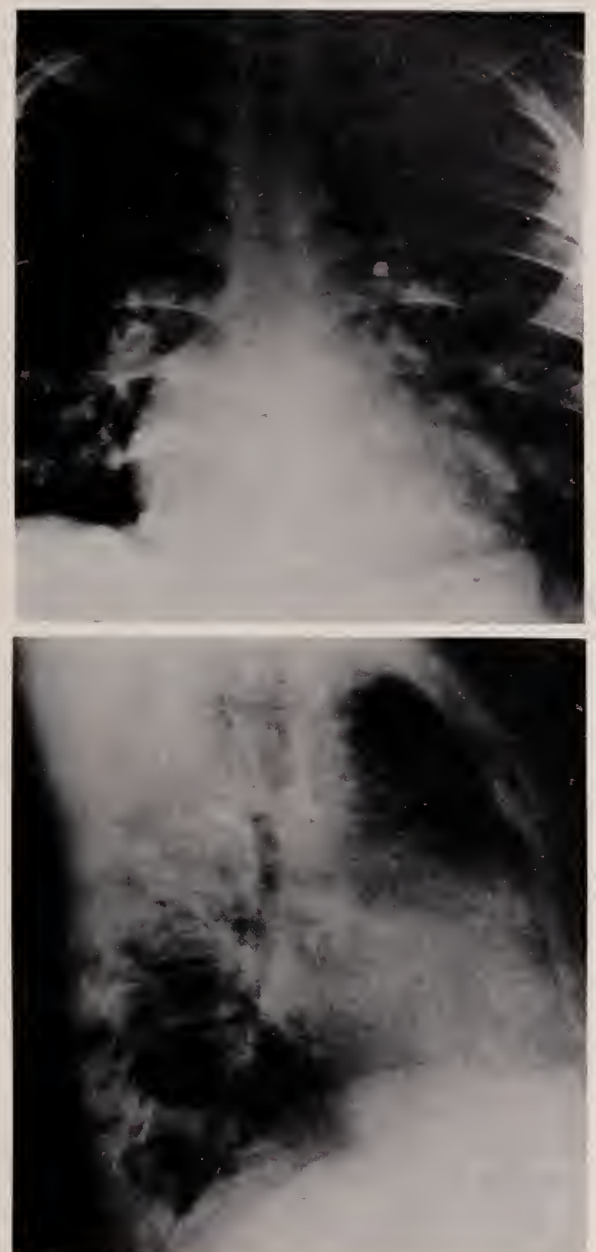


Fig. 1—Preoperative chest roentgenograms. Posterior-anterior and lateral views respectively, demonstrating probable biventricular enlargement and prominent pulmonary vasculature suggestive of left to right shunt.

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The electrocardiogram showed left anterior hemiblock (Figure 2).

On February 11, 1964 cardiac catheterization was performed. The findings were those of biventricular failure, moderate pulmonary hypertension, and a 72% left to right shunt at the ventricular level (Table). A selective left ventriculogram further confirmed the presence of this shunt.





Fig. 2—Postoperative chest roentgenograms. Posterior-anterior and lateral views respectively, demonstrating decrease in cardiac size and decreased prominence of pulmonary vasculature.

On February 18, 1964 surgical repair was undertaken using total cardiopulmonary bypass. A right ventriculotomy was done with demonstration of eight defects of the muscular septum, ranging from 2 mm. to 2 cm. in diameter. These were closed with interrupted mattress sutures and tied over 1/16 inch teflon felt. It was noted that several defects in the region of the apex had margins of friable, soft, muscle which held stitches very poorly.

Postoperatively, the systolic murmur persisted. On chest roentgenogram there was slight decrease in cardiac

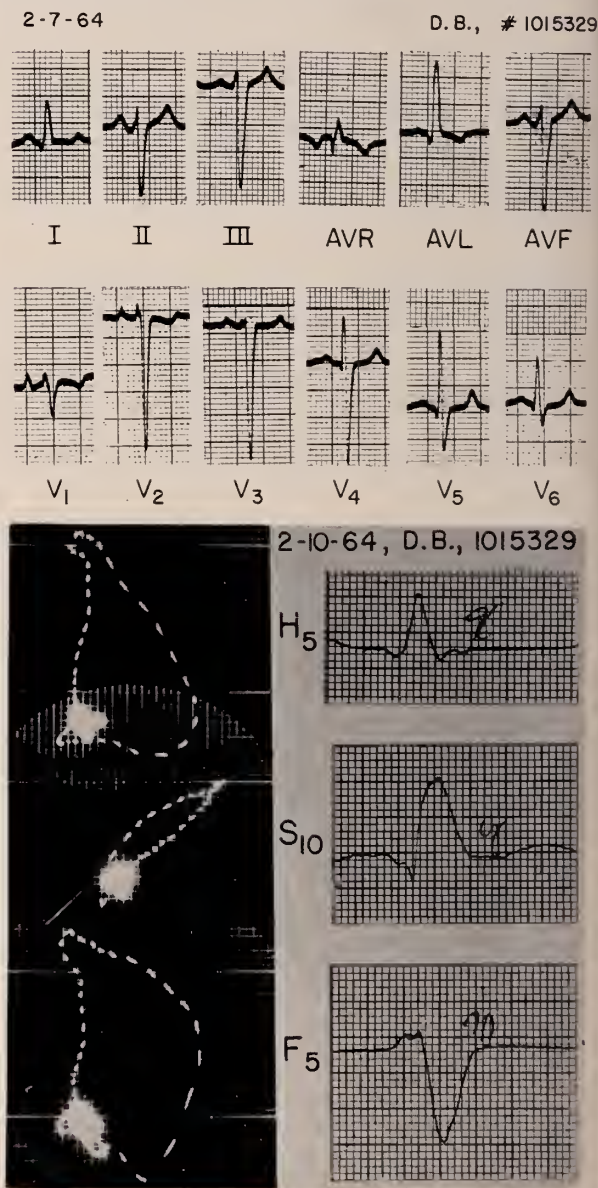


Fig. 3—(A) Preoperative electrocardiogram demonstrating left anterior hemiblock. (B) Preoperative vectorcardiogram (Schmitt's SVEC III lead system) demonstrating left anterior hemiblock and left ventricular hypertrophy. F_5 = frontal plane, distance between heavy lines = 1 millivolt; H_5 = horizontal plane, distance between heavy lines = 1 millivolt; S_{10} = left sagittal plane, distance between heavy lines = 2 millivolts; X = X axis; Y = Y axis; Z = Z axis.

TABLE
Cardiac Catheterization Findings

Date	Pulmonary Artery Pressure (mm Hg)	Right Ventricular Pressure (mm Hg)	Mean Right Atrial Pressure (mm Hg)	Mean Pulmonary Artery Wedge Pressure (mm Hg	Left to Right Shunt by Oximetry (%)	Left to Right Shunt by Indicator Dilution Curves (%)
2/11/64	70/30	70/10-20 (a wave)	13	25	69	72
3/10/64	40/20	40/0-12 (a wave)	9	12	72	71
11/5 /64	27/14	27/1-8 (a wave)	4		61	57
8/21/66	26/12	26/4-10 (a wave)	5	12	31	30

size and decreased prominence of the pulmonary vasculature (Figure 3). The electrocardiogram now demonstrated complete right bundle branch block and left anterior hemiblock.

On March 10, 1964 right heart catheterization was performed. The findings were borderline right ventricular failure at rest, a pulmonary artery pressure at the upper limits of normal, and a left to right shunt of 71% at the ventricular level (Table). The patient was treated with digoxin and a low sodium diet.

He was readmitted to the University of Minnesota Hospitals for further study on November 4, 1964. At this time there were no symptoms referable to the cardiovascular system. On physical examination the "a" wave was no longer prominent in the cervical venous pulsations. The systolic murmur was unchanged from preoperatively, and a faint apical mid-diastolic rumble persisted. The pulmonic component of the second sound was no longer prominent, and the protodiastolic gallop was no longer audible. The chest roentgenogram and electrocardiogram were unchanged.

On November 5, 1964 right heart catheterization revealed no evidence of cardiac failure at rest, a normal pulmonary artery pressure, and a 60% left to right shunt at the ventricular level (Table). Surgical intervention was refused by the patient.

During the subsequent two years he discontinued digoxin and was able to perform heavy labor as a construction worker without difficulty.

He was readmitted to the University of Minnesota Hospitals for re-evaluation on August 22, 1966. Right heart catheterization demonstrated normal pressures without evidence of failure at rest. There was only a 30% left to right shunt at the ventricular level (Table).

The patient was last seen on July 14, 1967 at which time physical findings were unchanged, and there were no symptoms referable to the cardiovascular system.

Discussion

Several previous investigators have suspected spontaneous closure of interventricular septal defects due to nonpenetrating trauma because of changes in physical findings or clinical course.[2,3,4] However, documentation of this phenomenon by serial cardiac catheterization has been achieved in only one other case.[1] This case of Rosenthal, Parisi, and Nadas was not operated upon, and, therefore, the number of defects could not be determined, although a single defect was suspected. In our case multiplicity of defects was proven at surgery.

Because the size of the left to right shunt was the same preoperatively and immediately postoperatively, it would appear that the surgical attempt at closure of the defects had little effect on the clinical course of this patient. A possible reason for failure of surgery could be the friable nature of the margins of the defects and their inability to retain sutures satisfactorily. In the future, perhaps a left ventricular approach and repair of defects from the left side might be more successful. In this way the pressure gradient between the two ventricles might prevent a patch from detaching from the margins of a defect, instead of causing detachment of a patch applied to the right ventricular aspect of the septum. Previous authors have utilized only a right ventricular approach.[5-10]

This case emphasizes the point that in carefully observed patients, early surgery is not always necessary and that medical management until the defect spontaneously heals may be the treatment of choice.

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Acute Laryngeal Trauma

Its Early Management

LAWRENCE W. DeSANTO, M.D.* AND AUBREY K. BROWN, JR., M.D.†

A SYSTEMATIC APPROACH to the management of acute laryngeal trauma is available in the medical literature.[1-5] Although early treatment is the keynote to successful rehabilitation, a scarred and crippled larynx frequently is discovered weeks after an emergency tracheotomy has relieved the urgency of the situation and other injuries have been treated.

The purpose of this paper is to discuss laryngeal injuries and to emphasize the need for enactment of an early treatment program that will permit functional rehabilitation of the upper parts of the respiratory and digestive tracts.

Principles of Management

The principles of management of an injury to the upper airway are the same as those applicable to other regions of the body: (1) recognition, (2) definition of the injury, (3) careful debridement, (4) early restoration of anatomic relationships, (5) repair of disrupted mucosal surfaces, (6) planned immobilization and (7) prevention or treatment of infection. To achieve total rehabilitation, an adequate lumen with a cartilaginous framework, functional muscles and joints, and an intact nerve supply are necessary. At times, total rehabilitation may be impossible; but it represents a goal that can be approached by application of these principles.

Report of Cases

Case 1

After an automobile accident in which she was thrown into the dashboard and then through the windshield, a 24-year-old woman (married and pregnant for six months) was admitted to the emergency room. The patient was cyanotic, severely dyspneic, and convulsing. Subcutaneous emphysema extended from her chin to the middle of her thorax. After an emergency tracheotomy, appropriate specimens for laboratory studies were obtained, and roentgenograms were made. The patient was taken to the operating room where a right pneumothorax was drained, and multiple facial lacerations were repaired.

Two days later, she was seen by an otolaryngologist because she was having difficulty in talking when her tracheotomy tube was occluded and liquids were being aspirated. Indirect examination of the larynx revealed that both vocal cords were fixed in the midline position, with an opening (1 mm) of the posterior portion of the glottis. Lacerations or dislocations of the supraglottic region of the larynx were not observed. A lateral roentgenogram of the neck demonstrated narrowing of the air shadow in the region of the cricoid cartilage and upper part of the trachea (Figure 1-A). Also, minimal deformity of the body of the sixth cervical vertebra was noted. Tomograms of the larynx showed obliteration of the laryngeal air shadow by soft tissue, asymmetry of the subglottic region, and fullness in the left subglottic region (Figure 1-B).

Four days after the accident, general anesthesia was employed through the tracheotomy tube, and the midline position of the vocal cords was verified by direct laryngoscopy. A bronchoscope was introduced to the level of the cricoid cartilage, where total obliteration of the lumen with disrupted mucosa and bleeding was observed. The neck was explored by enlarging the tracheotomy, and both recurrent nerves were identified and dissected to their terminal branching at the cricothyroid membrane. At this point, continuity was disrupted, and the terminal branches of the nerves were lost. The first tracheal ring and the cricoid cartilage had separated. The cricoid cartilage was in three large pieces (Figure 1-C). These cricoid fractures were reapproximated with stainless steel wire (No. 28) placed through the perichondrium. In the lumen, the viable mucosa was reapproximated. A skin graft of split thickness was taken from the right side of the abdomen and sewed around a stent made of sponge rubber; and the stent was placed in the disrupted lumen (Figure 1-D). Then, the trachea was drawn to the reestablished cricoid cartilage to provide a solid lumen around the stent. Prior to insertion of the stent, a small tracheo-esophageal fistula of the posterior wall was detected and closed. The stent was wired in place through the thyroid cartilage and secured with a fishline suture attached to the tracheotomy tube.

After the operation, the patient tolerated nasogastric feedings well. Within 10 days, she was swallowing normally. Twelve days after the laryngeal repair, the lumen was exposed (using the suspension laryngoscope), and the stent and excessive skin were removed from the reestablished larynx. At this time, the diameter of the lumen appeared adequate, but the anterior wall con-

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See editorial, page 348.

tained granulation tissue. For this reason, a second stent made of sponge rubber and covered with a finger cot was inserted and secured by a wire placed through the thyroid cartilage. Two weeks later, fluctuant swelling was noted around the wire on the left side of the neck. This infection was drained, cultured, and attributed to *Staphylococcus*. A suspension laryngoscope was employed, and the stent was removed. Although a bronchoscope (7 mm) could be passed through the lumen, some granulation tissue still remained on the anterior wall, and a third stent was prepared from an endotracheal tube. It was reinserted into the lumen and wired into place through the skin above the tracheotomy tube. The drainage in the neck quickly subsided when sodium cephalothin (Keflin) (500 mg intramuscularly every six hours) was employed. The patient was able to talk through the lumen of the endotracheal tube stent, and the plugged tracheotomy cannula did not cause difficulty. The tracheotomy tube remained plugged when she was discharged 30 days after admission.

On Jan. 21, 1968, the patient delivered a full-term boy, weighing eight pounds, one ounce. Four weeks later, the tracheotomy tube and stent were removed. When she was last examined on February 1, 1968, her airway was adequate and her voice was weak but functional. Both vocal cords remained paralyzed in the paramedian position with a glottic opening of 4 to 5 mm. Revision of the scar tissue of the neck (Figure 1-E) was planned within six to nine months.

Comment

In the presence of severe injuries to other organ systems, the damaged larynx can be overlooked



Fig. 1 (Case 1). (A) Lateral view of soft tissue of neck, with *arrows* indicating loss of air shadow at cricoid cartilage. (B) Anteroposterior tomogram, with *arrows* indicating narrowed laryngeal lumen. (C) Operative view of fractured cricoid cartilage. Hook is behind posterior lamina of cricoid. (D) Sponge-rubber stent prepared for insertion into laryngeal lumen. Note split-thickness skin graft with raw surface outward, which is sewed around stent. (E) Patient four months after operation. Anterior portion of neck after decannulation of trachea.

after a tracheostomy is established. Functional rehabilitation demands early definition of the airway injury.

Case 2

A 58-year-old woman was seen in the emergency room after an automobile accident in which she was thrown into the windshield. The patient was conscious, and respiration was normal. Her most apparent injury was scalp and forehead lacerations, but a contusion was noted on the anterior portion of her neck. Subcutaneous emphysema was absent. The lacerations were repaired, and the patient was admitted for observation.

Within eight hours after the accident, progressive dyspnea and subcutaneous emphysema of the neck developed. Indirect examination of the larynx was inconclusive. A soft-tissue roentgenogram of the neck was suggestive of a cricoid cartilage fracture (Figure 2). After tracheostomy and the administration of general anesthesia, the larynx was exposed with the use of a Jackson laryngoscope. Cordal motion was normal. The subglottic region of the larynx was narrowed by edematous mucosa and dislocated cricoid cartilage fragments. The fractures were easily reduced by passage of the laryngoscope through the lumen of the subglottic region. A sponge-rubber stent in the lumen maintained reduction. A skin graft was not necessary. One stent was removed in 15 days, and the tracheostomy tube was removed two days later.

The patient has a near-normal voice and a normal airway.

Comment

A serious, life-threatening injury can be present with little external evidence. The slight contusion of the neck heralded a severe airway emergency. Some injuries can be quickly and easily repaired without open surgery.

Discussion

The larynx, pharynx, and trachea are vulnerable to laceration, incision, contusion, penetration, crush, dislocation, and disruption; and the potential causes of such trauma increase with advances in warfare, transportation, industrial equipment, and household appliances. Whereas acts of violence, athletic contests, suicide attempts, tracheotomy, and irradiation must be added to a list of civilian injuries, the automobile accident remains the principal cause of the damaged airway. Sudden propulsion into a dashboard or front seat or through the windshield, with contact of the hyperextended anterior portion of the neck, is the usual mechanism of injury.* Fractures of the thyroid cartilage occur most frequently, whereas those of the cricoid cartilage occur less often. Acute obstruction of the airway may result from fractured cartilage, hematoma, arytenoid dislocation, or recurrent nerve damage with the vocal cords paralyzed in the adducted position.

In the emergency room, the diagnosis of an injury to the upper airway begins with systematic evaluation of the larynx after the urgent problems of hemorrhage, compromise of the airway, and shock are treated. All serious injuries will influence the voice or respiration or both. An abnormal or absent voice may be due to laryngeal or cerebral damage, but the larynx must be evaluated before any voice change can be attributed to a head injury. Stridor, noisy inspiration, dyspnea, suprasternal or infrasternal retractions, and acute or chronic hypoxia also demand evaluation of the upper airway.

External examination of the larynx may reveal minimal evidence of the underlying damage. Severe injury can occur after the direct hammering of the laryngotracheal complex against the cervical vertebrae without breaking the skin. Palpation of the neck may demonstrate loss of the normal landmarks of the thyroid or cricoid cartilages, deformity, dislocation, abnormal motion, crepitation, or induration. Subcutaneous emphy-



Fig. 2 (Case 2). Lateral view of soft tissue of neck. There is a retropharyngeal soft-tissue mass with presence of air in the retropharyngeal space.

*This type of injury is preventable to a degree by the use of the seat-belt and shoulder-harness arrangement that is now available in automobiles.

sema is not indicative of the severity of the injury.

The orderly evaluation of a laryngeal injury includes roentgenograms of the neck. A lateral view will provide information concerning the position of the cartilages and any distortion of the air column. Anteroposterior views and tomograms during phonation and rest may show mobility of the vocal cords, as well as fractures and dislocation. Aspiration may indicate a tracheo-esophageal fistula, but this abnormality may be due also to an ineffective glottic sphincter. Roentgenologic use of a contrast medium is necessary to rule out the possibility of a fistula, and iodized oil (Lipiodol) or meglumine diatrizoate (Gastrografin) are preferable to barium because they produce less reaction in the lungs. These agents are less viscous; hence, a small fistula is more likely to be visible.

Examination of the larynx by the use of an indirect mirror may be possible and helpful in the cooperative, conscious patient with a controlled airway. This indirect visualization provides knowledge of glottic motion, mucosal tears, hematoma, dislocation, and distortion of the lumen. As soon as the patient's condition permits, direct laryngoscopy and bronchoscopy should be done to complete the evaluation. Direct examination within 48 to 72 hours may be therapeutic in that cricoarytenoid dislocations can be repositioned and depressed, and nondisplaced thyroid or cricoid cartilage can be *ironed out* with the instrument.

Lynch's[5] classification of three types of laryngeal trauma provides a useful framework for the application of surgical principles in the repair of injuries of the upper airway.

A Type 1 injury is a wound from without that does not involve cartilage and is without laceration or damage. Such an injury includes blunt trauma or open wounds of the anterior surface of the neck and external portion of the larynx or trachea, without fractured or displaced cartilage or mucosa. Usually, debridement and primary closure of the wound in the neck is adequate treatment. Tracheotomy often can be avoided by careful observation of the voice and respiration in anticipation of laryngeal edema or hematoma. Hyoid fractures without mucosal tears belong to this category of injury. Unless the fracture is displaced enough to narrow the airway, careful observation is all that is necessary. The prognosis for an adequate airway and voice is good.

A Type 2 injury is a wound with laceration or injury of the interior surface without displacement. Laryngeal edema and hematoma are serious hazards in the Type 2 injury with open or intact cervical skin. Careful observation and a low tracheostomy at the first sign of respiratory distress are imperative before a desperate state is reached. A large hematoma needs evacuation to prevent fibrosis and loss of cartilage from perichondritis. Evacuation can be accomplished through a standard laryngoscope. Suspension laryngoscopy allows more flexibility by affording two-handed manipulation within the larynx and repair of lacerations through the mouth. With time and voice rest, mild hematoma and discoloration will resolve without evacuation. The voice and airway generally will be satisfactory.

A Type 3 injury is a wound with laceration and displacement of cartilage. A Type 3 injury may be fatal before emergency treatment is available. If the patient survives, a tracheotomy probably will be in place before the injury is defined. Throughout repair, a tracheotomy through the second and third tracheal rings should be adequate; however, if the tracheotomy has been made higher, it should be lowered. Fractures can be approximated by direct wiring with stainless steel sutures, and mucosal lacerations should be sutured with absorbable material.

If mucosa is missing, a split-thickness skin graft that is held in place with a compressible intraluminal stent provides several benefits: (1) prevention of low-grade infection of cartilage by providing a living dressing; (2) prevention of granulations and excessive scarring with contracture; and (3) hastening of the healing process. A graft will shorten the time a stent is required in the lumen, in addition to being well tolerated and causing minimal difficulty after operation if a hair-free area is chosen as the donor site. A compressible stent (sponge rubber) is cut to size, and the skin graft with the raw surface turned outward is sewn around the stent. The stent and graft are set in place through the laryngeal wound and are secured with transfixion wire. Also, the stent should be held to the tracheotomy tube with a fishline suture that is passed the full length of the stent and back to the caudal end. In 10 to 14 days, the initial stent should be removed through the mouth—care being taken not to

avulse the portion of the skin graft that is adherent to the reconstructed laryngeal lumen.

The period of stenting must be based on the extent of the injury and the status of the lumen at the time the first stent is changed. A minimal stenting period of three weeks has provided satisfactory results; however, eight weeks or more may be required. The final result in a patient with a Type 3 injury is often less than perfect.

The goal of decannulation is obtained more often than that of a normal voice. If the vocal cords are paralyzed, further efforts toward glottic rehabilitation for voice improvement or enlarging the glottic airway should be delayed for six to 12 months to be certain that all possible function has returned. Paralysis of the bilateral abductor muscles in a patient with an inadequate airway can be improved by arytenoidectomy and lateral repositioning of one vocal cord. An abductor paralysis associated with glottic air loss and a weak voice often can be improved by injection of Teflon lateral to one vocal cord to approach glottic closure during phonation.

Summary

Traumatic injuries of the larynx and cervical trachea vary from minimal hematoma to complex fracture, dislocation, or separation. Optimal rehabilitation of the airway and voice will occur if the injury is recognized early and if a program of management consistent with basic surgical principles of wound repair is instituted. In a few patients, the severity of other injuries may be responsible for delayed treatment of the airway, but the therapeutic priorities and timing should be determined through consultation with a laryngologist.

In most patients, a good airway should be an approachable goal, but chances for a good voice are less favorable if injuries are severe. All members of the team involved in managing the accident victim, especially the residents and interns who staff the emergency room, should be aware of the hazards of an injury to the airway and the essentials of early treatment.

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Myasthenia Gravis

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Myasthenia gravis is a chronic disease characterized by a variable degree of muscle weakness following voluntary use. Most commonly involved are the extraocular and other muscles innervated by the cranial nerves. Characteristically, the illness has a tendency to exacerbations and spontaneous remissions. Although in most cases certain muscles have a continually reduced function, the outstanding feature of the weakness is its relationship to activity. The chief feature of a pathologically rapid exhaustion of muscle power, linked to an abnormal slower speed of recovery, defines myasthenia gravis as unlike any other neurological process.

In the majority of cases the clinical manifestations are gradual in onset, but the disease may be ushered in suddenly with a sensation of general weakness. Ptosis, unilateral or bilateral, due to weakness of the levator palpebrae and diplopia due to involvement of the extrinsic ocular muscles are the commonest early manifestations. The weakness in the ocular muscles may occur in almost all combinations of functional disturbance. The day-to-day variability in ocular phenomena is one of the most diagnostic features. Pupillary abnormalities are almost never present. Visual fields and acuity are not altered.

Myasthenia does not always manifest itself initially in the extraocular muscles, since certain patients may present with speech or swallowing difficulty or other muscle group deficits but the extraocular muscles are affected at some stage in almost every patient.

As the disease progresses other muscle groups are involved. The classic picture is presented by the patient with bilateral ptosis resulting in a sleepy appearance; orbicularis oculi weakness with inability to close the eyelids; facial diplegia, rendering the face expressionless and apathetic; weakness of the circumoral muscles giving rise to the myasthenia snarl; and weakness of the masseters resulting in the mouth being constantly open. The voice becomes hoarse, nasal and gradually less and less distinct and complete aphonia may develop. In the more severe cases, dyspnea is a distressing symptom resulting from involvement of the respiratory muscles.

Once the disease has appeared the course may follow several patterns. There may be gradual extension of the involved areas to a steady state of weakness or there may be rapid deterioration. In one series of 220 patients, 32 percent died of the disease from three months to 25 years after onset. Eighty-five percent of these deaths occurred within six years. Schwab[14,15,16] reports that 10 percent of the patients died within 10 years of the onset.

Upper respiratory infections, grippelike illnesses and emotional tension are associated with exacerbations of the disease. Worsening of the condition often occurs during the premenstrual or postpartum periods.

Etiology

In view of the frequency with which thymic abnormalities are present in myasthenia, and the postpartum and menstrual relationships, many observers have concluded that this disease is basically an endocrine disturbance. No consistent dysfunction of an endocrine nature has been demonstrated and treatment with various hormones, including cortisone and ACTH, has not been beneficial.

Evidence is increasing that the thymus has an immunologic function. Moreover, the occurrence of neonatal myasthenia in offspring of myasthenic mothers which spontaneously subsides about seven weeks after birth indicate that myasthenia gravis may be a unique type of autoimmune disease. This is supported by the following:

1. Wilson and associates have thymic extracts which act as neuromuscular blocking agents;
2. Muscle biopsy shows a collagenlike disease;
3. Patients with myasthenia gravis have elevated gamma globulins and one fraction has been shown to bind to muscle;
4. Serum from myasthenic patients will cause lysis of frog muscle cells;
5. Serum complement is high in exacerbations of myasthenia and low in remissions;

6. Myasthenia is associated with known autoimmune problems (rheumatoid arthritis, acrocyanosis and systemic lupus erythematosis).

With the development of suitable recording methods for motor nerve stimulation and muscle recording, evidence is accumulating that the defect in neuromuscular transmission in myasthenia is due to an alteration in the acetylcholine mechanism. This could result from:

1. failure of nerve impulse to release a normal quantum of acetylcholine;
2. an excessive concentration of cholinesterase at the neuromuscular junction; or
3. elevation of the excitatory threshold of the motor end plate.

Thus, although it is agreed that the myasthenic defect is one of diminished acetylcholine effect, its precise mechanism remains controversial.

Medical Management

Medical management relies mainly on the anticholinesterase compounds neostigmine, pyridostigmine, and ambenonium alone or in various combinations. The alkyl phosphates, diisopropylflourophosphate, ethylpyrophosphate, hexaethyltetraphosphate, and octamethylpyrophosphoramide, once used, have proved too hazardous for clinical use.

Surgery and History

Since myasthenia has provided such a satisfying meeting ground for the clinician, physiologist and pharmacologist, it would be well to examine the historical highlights of this disease. Rufus, the Ephesian, is credited with giving first reference to the thymus. Galen called it an organ of mystery and felt it served as a cushion between the sternum and great vessels. The first description of myasthenia gravis came in 1671 from Thomas Willis, and in 1879 and 1893, Erb and Goldfam provided us with their classical descriptions.

The disease process was named myasthenia gravis in 1895 by Jolly and in 1912 Sauerbruch performed the first thymectomy for myasthenia gravis, a treatment which was unfortunately forgotten for many years. The next important step came in 1920 when Loewi and Dale developed their chemical theory of junctional transmission and in 1934 Mary Walker, after hearing a lecture on anticholinesterase therapy for curare poisoning gave physostigmine to one of her myasthenia patients. Thus, began the medical therapy for this disease.

In 1935 Viets and Schwab described a diagnostic test for myasthenia using an anticholinesterase and in 1939 Alfred Blalock presented his notable account of removing a thymoma from a myasthenic who recovered without neuromuscular disease and thereupon revived Sauerbruch's operative procedure for myasthenic patients. In 1946 Keynes reported on 51 thymectomies for myasthenia. Since that time there has been a multiplicity of reports from large institutions with large series of patients condoning and condemning thymectomy for myasthenia gravis.

Westerberg et al. stated that thymectomy was not of great value or it would not be so difficult to determine whether or not it is useful. As late as 1962, Ferguson reported a series of 145 patients with a small number of operations. He concluded that "when one considers the natural tendency of myasthenic gravis to remit and relapse it is extremely difficult to assess the precise role of the thymus in the symptomatology of myasthenia and the potential value of thymectomy itself." Simpson, on the other hand, after analysing 404 cases feels thymectomy is indicated in almost every case of myasthenia.

That there should be some dispute concerning therapy for a disease with such protean manifestations as myasthenia is quite understandable. Furthermore, when comparisons are made among different reported series a uniform classification must be used in the tabulation of results. Also, one must compare patients of similar age range because operated groups generally include many young patients while the nonoperated groups contain more older patients.

Probably the most important criterion for comparison of thymectomy series is to differentiate patients with thymomas from those without. Most of the early reports from this country included thymomas. Myasthenia associated with a thymoma is a far more severe disease, than that associated with a thymus showing hyperplasia of the germinal centers or so-called "normal, but enlarged" thymus.

Simpson in 1958 reported on a group of myasthenic patients aged 16 to 35, without thymoma, and treated by thymectomy and anticholinesterases. His evaluation of the therapeutic result depended on a comparison of the pre- and postoperative state with respect to signs, symptoms, exercise tolerance and drug requirements. He classified the results as A, B, C, or D and care-

fully explained what each letter represented so that others could similarly classify their patients. He hoped that such a classification would lead to a unified body of data so that statistical confirmation of results could be done.

Simpson found that fewer women die of myasthenia gravis if their thymus is removed than would be expected if treated with neostigmine. Also, a higher proportion of operated patients were greatly improved. These differences are significant to the .05 level. The greatest improvement tended to occur in the youngest patients with the shortest preoperative courses. These differences, however, are not sufficiently marked to discount chance effects.

In females, preoperative severity of the myasthenia measured objectively by neostigmine requirements did not appear to be a significant factor in affecting the course of survivors; although those who died were those who tended to be on higher neostigmine doses. Similar trends were found in the male series, but none of the differences were of a magnitude to exclude chance. However, the fact that the course of males, after operation, was in the same direction as female suggests that males do benefit in the same way as females from thymectomy.

Simpson compared his results with those from the Mayo, Boston, and Baltimore series after he had reclassified their results into his A, B, C, or D system. He also omitted those patients with thymomas. By doing this he was able to show that there is general agreement on the mortality rate and extent of remission in these American series similar to his own. Although the American centers did not consider that males are significantly benefited by thymectomy, here again patients with thymoma were included in the thymectomized group.

With regard to age, the Mayo Clinic series agreed that the age of onset did not significantly affect the response to thymectomy. An unexpected finding from Simpson's results is that the deaths occurring despite thymectomy were in a group whose characteristic age of onset, age at operation and duration of symptoms were similar to those of the group deriving the most benefit from thymectomy. Of those who died, whether thymectomy carried out or not, it appears that the crucial period is from four to seven years after onset. These patients are most difficult to control with neostigmine. Simpson also stated that even though occasional relapses were noted it was common for improvement to be progressive for several years after operation. Despite all the data in Simpson's report, we still do not have all the criteria to allow us to predict the effect of thymectomy in the individual patient. Nonetheless, it is clear that thymectomy should be seriously considered in all cases in which myasthenia is not confined to the ocular muscles. When only the eyes are involved, Ferguson et al. have reported on 69 patients who for the most part did well on medical treatment.

Thymomas

In patients with thymomas, which comprise from 10 to 35 percent of myasthenic patients, depending on the series, the mortality rate is not lowered by thymectomy and regardless of the mode of treatment mortality is up to 80 percent in some series.

The mean age of onset for myasthenia with a known thymoma is about 40 years for males and females compared to 25 to 30 years for non-tumor patients. Keynes feels these tumor patients are harder to control medically and Simpson has shown that the neostigmine requirements in his group of thymomas was 25 to 50 percent higher than his non-tumor patients.

Both Boyd and Keynes stress that the margin between benignity and malignancy is very fine with thymomas and advocate aggressive surgical therapy for all thymomas thought to be resectable since histologic benign lesions often involve the pleura and pericardium. Keynes prefers preoperative radiation while Boyd uses postoperative radiation. Others use only radiation instead of thymectomy.

Preoperative Care

The exact dose of anticholinesterase required preoperatively should be determined accurately so that overdosage in the postoperative period is avoided. Deep breathing and coughing should be practiced before operation. Cigarette smoking should be stopped.

Postoperatively

A tracheostomy should be performed in the operating room in almost all patients. Care must be taken to avoid a cholinergic crisis from too much anticholinesterase with resultant excessive

pulmonary secretions, muscle weakness and respiratory insufficiency. Postoperatively, signs of cholinergic crisis are muscarinic effects associated with compensated respiratory function, whereas preoperatively muscle cramps, diarrhea, nausea, and vomiting preceed the respiratory difficulties. It is imperative that trained personnel observe these patients postoperatively to recognize the signs of respiratory insufficiency.

Summary

Myasthenia gravis is a chronic muscle disease of variable weakness characterized by rapid muscle exhaustion and slow recovery. Much evidence exists for an autoimmune etiology although other evidence points to a hormonal imbalance. Medical therapy consists of anticholinesterase administration while surgical therapy relies on thymectomy. Recent, more precise evaluation of patients indicates that males and females without thymoma respond to thymectomy. Myasthenic associated with thymoma is more severe and responds poorly to drugs and thymectomy.

Preoperative evaluation and preparation are essential for safe postoperative management. Care must be taken to avoid giving too much anticholinesterase because toxicity signs can be confused with signs of insufficient medication.

Acknowledgement

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There are but two ways of rising in the world: either by one's own industry or profiting by the foolishness of others—La Bruyère

Special Article

Psychiatric Training in a Department of Obstetrics and Gynecology

IRVING BERNSTEIN, M.D.*

A PSYCHIATRIC teaching program in the Department of Obstetrics and Gynecology at the University of Minnesota has been in operation since 1951. The aim is to offer students and staff experience in the recognition and treatment of the psychosomatic problems that present to the practicing physician.

In an obstetrical-gynecological service the connection between feelings and complaints is easily demonstrated. The relationship is often evident between feelings of insecurity and dysmenorrhea,[1] feelings of rejection and nausea and vomiting of pregnancy,[2] inability to compete and hypochondriacal complaints,[3,4] anger and sexual incompatibility, depression and abdominal discomfort. Using obstetrical and gynecological patients for psychiatric teaching does not generate the anxiety in students that usually occurs upon their exposure to the psychiatric patients routinely presenting on an inpatient service in a medical school hospital. Hill states "Utilizing severely ill psychiatric patients to teach medical students is unwise."[5]

Instruction for medical students was accomplished through five to seven weekly one-hour seminars, participation in weekly grand rounds, and the provision of consultative service and psychiatric care on the obstetrical-gynecological service during an eight week clerkship.

To establish such an integrated program, a psychiatrist with an interest in teaching, who enjoys identification with the general practice of medicine, must be available. He should be able to handle both the negative and positive feelings about psychiatry which present in students and staff. Initially, the program was accepted with some reservation by John McKelvey, Chairman of the Department of Obstetrics and Gynecology. In the following years, over-acceptance and inability to satisfy requests for service became problems.

Psychiatry was shown to be similar to general medicine in that pathology was demonstrated, treatment affected and disposition made by a psychiatrist, usually without the assistance of ancillary services. Basic psychiatric skills were taught. All students, graduate or undergraduate, were expected to become adept in interviewing a patient in a manner that reduced anxiety and utilized the patient-doctor relationship to the utmost. The students were taught to be noncritical, noncensoring, and accepting of their patient's feelings, to accept resistance and set limits, and to give reassurance only when indicated.

The importance of establishment of a personality evaluation in every patient was emphasized. Students were taught the initial history should include information about the patient's past and current life situations, without the patient's feeling an irrelevant and intrusive psychiatric inquiry was being made. After the initial interview each patient was to be psychiatrically categorized as normal, neurotic, psychotic, psychopathic, or organic. The student was shown that the personality of the patient can greatly determine the effectiveness of the treatment of a disease process. This could be demonstrated vividly in the treatment of a pregnant diabetic, whether the patient was neurotic, psychotic, psychopathic or organic. Obsessive compulsive pregnant diabetics respond well to treatment; on the other hand, psychopathic pregnant diabetics respond poorly.

To emphasize the value of psychiatric expertise, symptoms had to be eradicated or alleviated. Effective management of nausea and vomiting of pregnancy, urinary retention following delivery, vulvar itching, impotence, infertility, frigidity, and generalized hypochondriasis impressed the staff and students, and encouraged them to become personally involved in treating patients with such symptoms.

Positive feelings toward psychiatry developed in the department staff and the majority of the students participating. Some of the students decided to become psychiatrists, and eventually did. A number of obstetricians reported a better understanding of their patients because of the

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psychiatric experience they obtained during their residency.

In 1969 the University of Minnesota Medical School instituted a dramatic change in its curriculum.[6] It was divided into three phases, A, B, and D. Phase A, consisting of three quarters, and Phase B, consisting of five quarters, constituted the core program. After completion of the core program, the student may graduate in either three or five quarters with an M.D. degree. Phase D is essentially elective.

It became possible to graduate from the Medical School with very little practical experience in psychiatry. In Phase A, a course in Behavioral Science is offered which consists of 60 hours, of which 30 hours is experimental psychology. All instruction is given by non-medical personnel—psychologists and sociologists. In Phase B, a 50-hour lecture course called *Behavior of Man* is offered under the direction of a psychiatrist. In 1971 an 18 hour course in Human Sexuality was added to the curriculum. This is the extent of the required psychiatric exposure at the University of Minnesota and thus some students will be able to complete medical school without examining and being involved with the treatment of a single identified psychiatric patient. Kaufman[7] deplores such deemphasizing of psychiatry in medical schools in a recent paper in the *American Journal of Psychiatry*.

With this curriculum modification, psychiatric teaching in the Department of Obstetrics and Gynecology had to change because much of the teaching became elective. Two courses are now offered. One consists of one to three students choosing to be assigned halftime or fulltime to the author in a preceptorship for a maximum of six weeks during Phase D. The other consists of a ten-hour lecture course called *Medical Aspects of Human Sexuality* which meets weekly during Phase B. The preceptor experience with the medical students has been stimulating for both students and teacher. The course in *Medical Aspects of Human Sexuality*, on the other hand, has been unsatisfactory for most of the students and the instructor, mainly because the students registered, thinking they had no responsibility to do anything for the course.

Most students who attended the lecture course and took the Phase D clinical elective came with the intention of learning the "tools of the trade," such as hypnosis, and did not want to be involved as much with obtaining scientific insights. These were the students having some interest in psychiatry. It is assumed the others were not as interested in psychiatry and thus, received less exposure to clinical psychiatry. In other words, those students who might be in most need of acquiring psychiatric skills were getting the least training.

It appears that the new curriculum in the University of Minnesota Medical School, with its lessened emphasis on the emotional aspects of illness, will result in less efficient care of both psychiatric and non-psychiatric patients and reduce the number of students choosing psychiatry as a specialty.

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Meetings

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the 3 phases of Eve



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Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

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Editorials

The Patient with More than One Cancer

CANCER IS AN exceedingly common disease. As our population increases in longevity and hopefully the treatment of malignant disease becomes more successful, it is to be anticipated that an increasingly large proportion of luckless individuals will be stricken with two or more primary and independent malignant neoplasms.

In 1932 Warren and Gates[2] were able to collect only 1259 cases of multiple primary malignant neoplasms from the world literature. By 1966 this total had swelled to over 20,000. During a single decade of Mayo Clinic practice we counted 1909 patients with more than one histologically confirmed primary cancer including 50 cases with cancers primary to three different tissues, two cases with cancers primary to four different tissues, and one case with cancers primary to five different tissues.

As Doctor Spanos and associates* have indicated in earlier pages of this issue, there is a striking predilection to develop a second cancer in a tissue that has already given rise to neoplasia. This phenomenon is grossly evident in the very frequent multiplicity of cancers of the skin, the oral cavity, the large bowel, the urinary tract, and the vulva, vagina, and anus, as well as in the very common bilaterality of breast cancer. The tendency to multicentricity of epithelial malignant disease is perhaps best explained by the words of Willis: "In human as an experimental carcinogenesis the effective stimuli are applied, not to one cell or one small group of cells, but to a more or less extensive area of epithelial tissue. All of the epithelium in that area is acted upon similarly, though of course, usually not equally. Neoplasia will commence where stimuli have been maximal, but the neoplastic process will later be manifested by neighboring tissue that was subjected to the same original stimuli." From a practical standpoint carcinoma should be regarded as a disease of an entire tissue rather than a single tumefaction. In surgical treatment, the entire tissue should be excised if this can be accomplished without disabling functional or cosmetic impairment and without prohibitive surgical risk. If this cannot be done, the patient must then be impressed with the vital importance of frequent follow-up examinations.

With regard to multiple neoplasms of different tissues of origin, Doctor Spanos and his coworkers have judiciously refrained from joining into the statistical parlor games that are so frequently being played with multiple cancer data. In spite of the large number of retrospective studies replete with comparative age specific incidences, etc., it can be stated without fear of valid contradiction that there is no evidence that the patient who has developed cancer is any more likely, or indeed any less likely, to develop a second cancer in a different tissue than is the patient who has never had cancer at all.

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*See page 318.
†Mayo Clinic and Mayo Foundation, Dept. of Internal Medicine.

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Muscae Volitantes

MUSCAE VOLITANTES, flies flying or flies that fly, are the floating specks of various shapes and size that people see in their field of vision. A patient will say, "What is this tiny object which I see but can not look at, because when I look at it, it darts away?" Because these floaters seem to fly about, they are likened to flies. These "flies," flitting in one's field of vision, may be as annoying as the sticky walking flies which one encounters in warm countries such as the Middle East where flies will walk on the merchant's face in the bazaar and seem oblivious to the brushing hand of the busy bargainer.

Muscae volitantes are vitreous floaters which cast a shadow on the retina and move with each eye movement. The motion of the shadow cast by the floater has a quick component of one to two seconds and a slow return component of from 5 to 12 seconds, depending on the physical state of the vitreous. Vitreous floaters may be discovered suddenly by the patient and this discovery may be very alarming. When the patient realizes that this is not an insect or a hair or thread caught in his glasses frame but that this is something wrong with his eye, he may become quite concerned. In practically all instances these patients can be reassured and told that although annoying, the floater they see represents no serious eye pathology.

There is the occasional person, however, as pointed out by Robertson,* who does have a retinal tear which is related to the vitreous floater pathology. Along with the vitreous floater there frequently are light flashes, and these are a little more common when the vitreous floater is associated with a retinal tear than when there is no retinal tear. As pointed out by Robertson, retinal tears frequently lead to retinal detachment. For this reason all patients with vitreous floaters must be examined carefully, even though serious retinal pathology is found in only a very small percentage of cases.

Muscae volitantes are but one of several entopic phenomena associated with the ocular media. Any object in the ocular media situated anterior to the retina can be seen entopically if it has an optical density different from that of the optical media. Floating bodies near the fundus, especially if large, are easily seen and may be quite annoying. They are most easily seen when viewed against a white page or light sky. No special optical aid is needed to see this entopic phenomena. To observe opacities in the interior part of the eye, one must use an optical aid which in effect causes parallel rays of light to pass from the region of the opacity to the retina. The opacity in these parallel rays then casts a shadow on the retina which is seen by the patient. A simple method which is used to produce parallel rays of light passing from the front of the eye to the back of the eye is to place a pinhole .1 mm. in diameter or smaller in a piece of paper, and then place this pinhole at the anterior focal point of the eye (15.7 mm. anterior to the cornea). A bright light is viewed and a shadow of the opacity falls on the retina. This entopic field is bordered by the shadow of the pupillary border, and the size of the pupil and defects in the pupillary border can be studied. If the pinhole is moved closer to the cornea than the anterior focal point of the eye, the shadow of the opacity in the media is magnified. If the pinhole is moved farther from the eye than the anterior focal point, the shadow is minified. The most important entopic phenomena are (a) opacities in the tear layer, corneal surface, and cornea (b) lenticular opacities and (c) muscae volitantes.

The presence of visible particles in the eye has been noted in the very old medical literature. Dechales (1690) and de la Hire (1694) speculated about the nature of muscae volitantes of the vitreous body. Probably the most brilliant observer of the subjective phenomena of vision who ever lived was Johannes Evangelista Purkinje (1781-1865), professor of physiology at Breslou and later at Prague. Sir Stewart Duke-Elder points out that Purkinje's contributions came while he was working in the attic of his house, and ceased when he was presented with the first State Physiological Institute in the world in 1839. Duke-Elder remarks, "It is only rarely that the true spirit of science thrives in an atmosphere of luxury."

Richard C. Horns, M.D.
Minneapolis, Minnesota

*See page 314.

Urinary Tract Infections

THE PAPER BY John M. Matsen in the March 1972 issue* of MINNESOTA MEDICINE brings us a thorough review of diagnostic procedures and therapy for urinary tract infections as seen by an experienced clinical microbiologist. The importance of urinary infections is emphasized by the fact that by age 60 as many as 10% of women will have had at least one episode. There is also the very real danger that the infection may ascend from the urinary bladder to the kidney. The clinical diagnosis of lower urinary tract infections is quite simple, but the identification of pyelonephritis in bacteriuric patients is more difficult, often requiring pyelography and tests of renal tubular concentrating ability. Patients with recurrent urinary tract infections should also have a voiding cystourethrogram in order to detect any lesions obstructing the bladder neck with significant vesicoureteral reflux, which may require surgical relief.

The recognition of high grade bacteriuria has been made relatively easy in recent years by the quantitative culture of a midstream aliquot of urine obtained by cleancatch, a method which is particularly easy in males but also applicable to females after proper cleansing of the vulva. The urine specimen should be promptly divided into separate portions in clean containers for microscopy of centrifuged sediment and gram stain of unsedimented urine, as well as a sterile container for quantitative culture for aerobic bacteria. These tests are sensitive, economical and specific, if properly done. Identification of the common causative organism usually is quickly made if several selective agar media are used. Susceptibility to antibacterial drugs can be easily determined on most bacterial pathogens by the Kirby-Bauer disc method. The test is particularly helpful in selecting therapy for patients with recurrent bacteriuria.

Chemotherapy for bacterial cystitis should be specific for the causative organism and need only be continued for a few days. The clinical result should be followed by further quantitative urine cultures. One has available numerous effective therapeutic agents, perhaps the least costly is sulfasoxazole. The treatment of acute pyelonephritis is more difficult, because the patients are often quite ill, and the bacteriuria is frequently due to more resistant bacteria, especially in patients developing infections after instrumentation. The choice of chemotherapy must be made with the aid of susceptibility tests, renal function tests (serum creatinine) and appropriate history to elicit possible drug allergies.

The treatment of patients with recurrent bacteriuria and chronic pyelonephritis is often quite unsatisfactory. One may use methenamine salts with urine acidification to suppress bacteriuria over prolonged periods, but evidence is conflicting as to the ultimate efficacy of chemotherapy in preventing relapses in these cases.

Finally, the prostate gland has recently been receiving some well-deserved attention as a possible source of recurrent bacteriuria in adult men. Stamey and others have shown that the prostate is often poorly penetrated by antibiotics. The best penetration seems to be obtained with sulfasoxazole, erythromycin or one of the tetracyclines. Acute prostatitis usually responds more quickly to chemotherapy than does chronic prostatitis, which is often not associated with infection with the common aerobic bacterial pathogens.

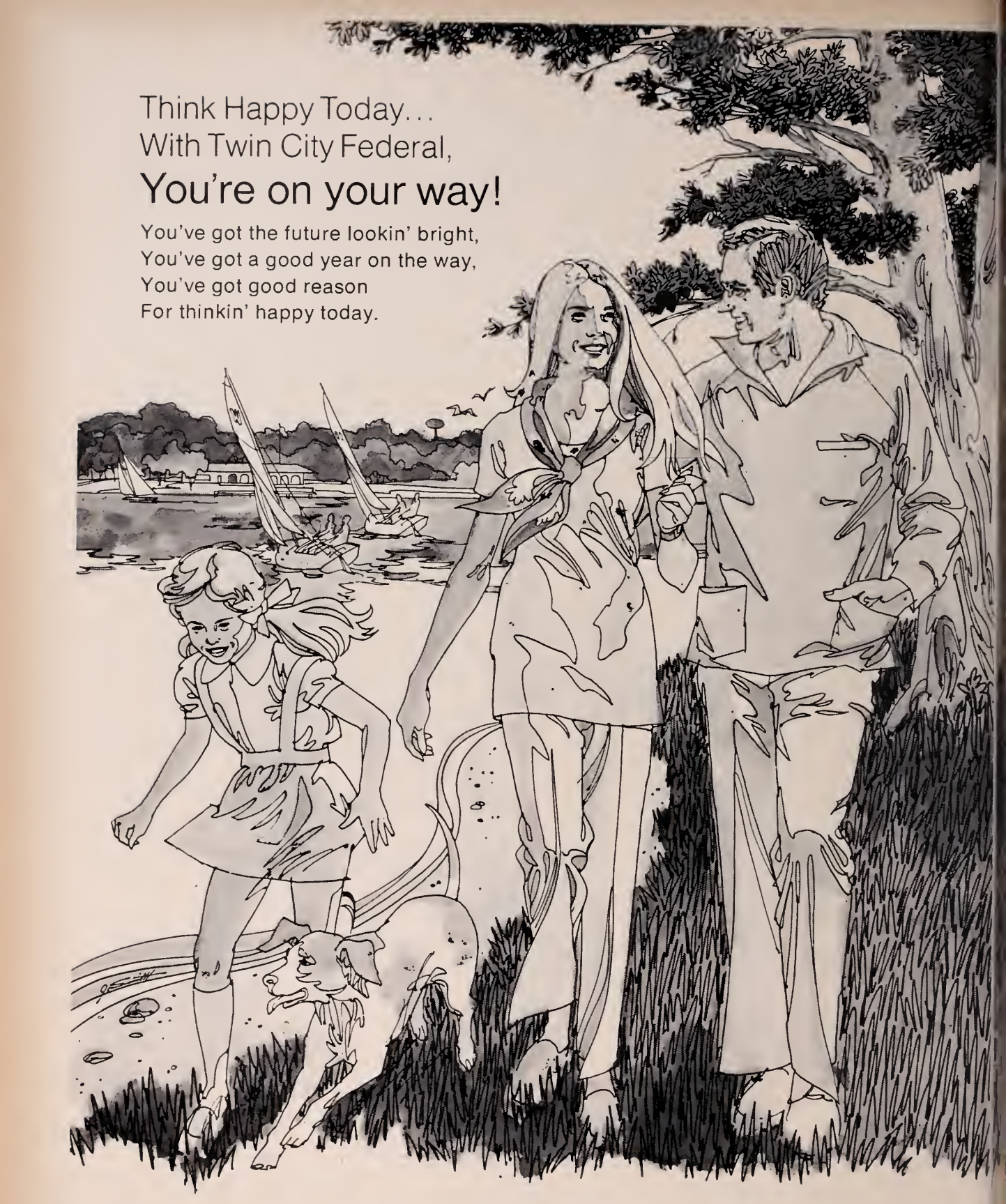
Wendell H. Hall, M.D.†
Minneapolis, Minnesota

*See page 200.

†Veterans Adiministration Hospital. Minneapolis.

The advertising quack who wearies
With tales of countless cures,
His teeth, I've enacted,
Shall all be extracted
*By terrified amateurs.**

*W. S. Gilbert, "My Object All Sublime," **The Mikado**, 1885.



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To some degree, the practice of medicine is controlled by concepts of disease and habits of treatment which are the products of hearsay from one physician to another or in some instances based on data passed even from one generation to another. A striking example is the supposed benefits of prolonged bed rest in a variety of illnesses, benefits which, in the last decade, have not withstood a more critical examination.

It is a widely held concept that gallbladder disease is more common in patients with heart disease and that patients with heart disease and gallbladder disease are apt to derive striking benefit from cholecystectomy. There has been evidence, particularly from autopsy series and a variety of case reports, to support this concept. The evidence is reviewed at some length in an article by Dr. John Anderson published in the March issue of Minnesota Medicine.*

That there is some kind of specific relationship between biliary tract and coronary heart disease, is not, however, universally accepted. Forrester et al.[1] from the Peter Bent Brigham Hospital found no significant increase in the incidence of gallbladder disease among a group of patients with coronary artery disease diagnosed angiographically. Neither did they find that gallbladder diseases contributed to the appearance of angina pectoris or cholecystectomy relieved its occurrence. In a review of the literature up to 1969, Friedman[2] found evidence for any relationship at best "meagre." With regard to the ECG abnormalities, Birbaum and Braun[3] found the incidence in patients suffering from cholelithiasis no different from that in a control group.

The truth of the matter remains in doubt. More information is needed. There are obvious benefits to be obtained from cholecystectomy in patients with coronary artery and gallbladder disease. Not least of these is a relief from the diagnostic confusion as to whether, in any given instance, the patient is having a heart or a gallbladder attack. However, that such surgery contributes to the relief of angina, or somehow ameliorates progression of the heart disease is not certain. Recommendations for this particular operation should possibly receive no higher priority than would be given in any group of high risk patients.

Paul Lowry, M.D.
Minneapolis, Minnesota

*See page 211.

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University of Minnesota Urology Department

The urology department of the University of Minnesota has received a $225,000 grant from the National Institutes of Health. The three-year grant will be used to support a study of genitourinary neoplasms, especially cancer of the kidney.

Dr. Elwin Fraley, department chairman, received a $140,000 grant three years ago from the Royal A. and Olive W. Stone Memorial Fund of the Minnesota Medical Foundation to establish a cancer research program in the department of urology. Dr. Fraley explained that the NIH grant, the first such given to a urology department, would be used to combine basic and clinical research efforts.

The laboratory team includes Dr. Thomas Hakala, Dr. Arthur Elliot, Dr. Anthony Castro and Dr. Ricardo Gonzales.

Laryngeal Trauma

SEVERE TYPES of laryngeal injuries are occurring frequently. This is due mostly to automobile accidents, but a new cause is the snowmobile. In the car, the larynx is crushed between the steering wheel or dashboard and the hyperextended cervical spine which acts as a perfect anvil. With the increased use of snowmobiles comes an increasing number of mutilating injuries and deaths. Maxillofacial and laryngeal injuries are seen more frequently due to snowmobiles.

Although some minor soft tissue injuries can resolve spontaneously, the more severe injuries with fracture and disruption of contour almost always heal with a severe limitation of the airway and vocal function. It is difficult to differentiate between the minor soft tissue injuries and the more severe injuries without a direct laryngoscopic examination or even at times an open reduction of the larynx. It is critical as DeSanto and Brown* point out that this distinction is made early, because the results are vastly better with proper treatment at an early time. If a watch and wait attitude is developed, the larynx may heal in a way that can never be corrected adequately even with multiple procedures. The patient may need to wear a permanent tracheostomy and have very limited vocal function.

These types of injuries occur commonly in remote areas. Emergency measures including tracheotomy are performed, but because of the severity of other injuries, or inattention to the larynx, the laryngeal injury is overlooked. Subcutaneous emphysema, hoarseness, pain, dysphagia, airway obstruction, or irregularity of the laryngeal cartilages by palpation are clues that must be fully evaluated.

Treatment consists of reduction of fractures on injuries to restore normal anatomy and splinting over a stent or a tube much like an andotracheal tube that is left in place for two weeks or three months depending upon the severity of the injuries.

Curtin, Holinger, and Greeley[1] reported 82 cases of laryngeal fracture. All but two had cicatricial stenosis of the larynx by the time they were seen. Fitz-Hugh, Wallenborn, and McGovern,[2] however, reported 28 cases of which 25 were treated early. Of these patients, 16 had good airways and 14 good voices out of 24 completed cases.

Some of the patients of Curtin, Holinger, and Greeley were undoubtedly denied early treatment because of the severity of their other injuries. It is fair to speculate that many, however, were denied early treatment because of the fact that the attending medical personnel were unaware of the importance of early treatment.[3]

John S. Huff, M.D.
Minneapolis, Minnesota

*See page 328.

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*"Aff-ffected m-madness w-will p-pass for w-wit w-with nine-ninet-teen out of t-twenty."—"And affected stuttering for humour: replied our landlord, tho', God knows, there is an affinity betwixt them."**

*Tobias Smollett, "The Expedition of Humphry Clinker" (1771).

Letter to the Editor

Dear Editor:

I was interested in your recent article in MINNESOTA MEDICINE February 1972 edition—"How Do I Take Care Of My New Baby, Doctor"? by Dr. A. G. Miller.*

As a practicing dermatologist, I question just a little of Dr. Miller's advice regarding skin care. He mentions that hexachlorophene is a halogenated salicylanilide. This is untrue. Hexachlorophene is a chlorinated bisphenol, and though related, is not a member of the salicylanilide group. Furthermore, Ivory is suggested as a good soap for routine skin care of children on the grounds that is not as drying as the germicidal soaps. Though the germicidal soaps do tend to produce drying of the skin with prolonged use, Ivory soap is in fact one of the most drying soaps available, and even though "pure", it is probably not the most desirable soap for routine use. In general, superfatted soaps such as Basis, Oilatum, Petrophyllic, etc. are probably more ideal. Note is made by Dr. Miller of the possibility of photocontact dermatitis after the use of germicidal soaps. Though this is certainly a fact in adults, not one single case of photocontact dermatitis to the germicidal soaps has been reported in infancy.

Peter S. Herman, M.B. B.S., M. Sc.,
Sherbrooke, Quebec, Canada

*Page 145.

Cover Photo

"Nature's Still Life"

Dr. Donald C. Bell, internist, spends a great deal of time hiking with his family, and it is not unusual to find the Bell family spending their vacations in the beauty spots of the nation. The cover photograph was taken while the family was hiking in the Rocky Mountains National Park in north central Colorado. It was about mid-day when the family chanced upon this beautiful first sign of Spring.

Dr. Bell practices at the Fairview Hospital and the Metropolitan Medical Center in Minneapolis.

Meetings

Medical Seminar dealing with the adolescent patient, Saturday, April 15, 9 a.m. to 5 p.m. Fairview Hospital and St. Mary's, Minneapolis. $10 fee will include luncheon. Contact Dr. Dorothy Bernstein, Director of Adolescent Treatment Unit, Fairview Hospital. Open to all physicians. Students and residents are invited as guests at no fee but advance registration requested.



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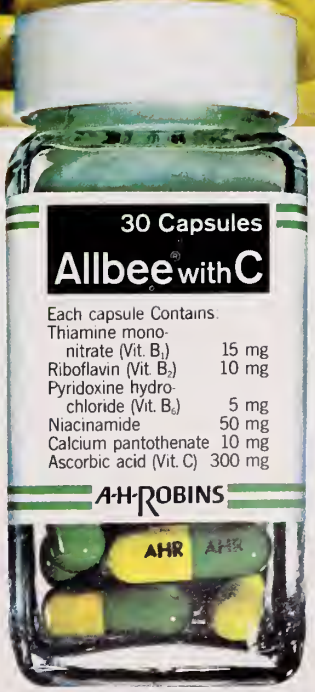


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Viewing Box

An Unusual Complication of Cystourethrography*

ALEXANDER S. CASS, M.D.† and ROGER VITKO, M.D.†

CYSTOURETHROGRAPHY HAS become an important procedure in the investigation of urinary tract infections in children and in the evaluation of upper urinary tract deterioration with myelomeningocele.

The following report shows that even a simple procedure can have complications.

Case Report

A 12-month-old male with a repaired lumbosacral myelomeningocele, had a cystogram (Figure 1) as part of a regular evaluation for the urinary tract complications of myelomeningocele.[1] The 8 Fr. soft plastic feeding tube, used as a catheter to introduce the dye into the bladder, could not be withdrawn from the urethra despite the use of reasonable traction. The child became markedly distressed and plain lateral radiography of the pelvis (Figure 2) revealed the tube to be doubled up in the urethra. Under general anesthesia the impacted doubled up tube was pushed back into the bladder and was then easily withdrawn through the urethra. The child voided normally when awake.

*Supported by the Medical Education & Research Account, Gillette Childrens Hospital.

†Urology Service, Gillette Childrens Hospital, St. Paul, Minn.

See page 324 for References 1-2.



Fig. 1—Cystogram showing the tube curved in the dome of the bladder, crossing itself at the bladder neck and its end engaged in the posterior urethra.



Fig. 2—Diagram showing tube doubled up in the urethra.

Discussion

Kjelberg reported two technical complications in 1,770 urethrocystographic examinations; an unduly soft catheter coiled up in the urethra requiring anesthesia for its removal and the tip of a many times sterilized catheter broke off in the bladder requiring operation for its removal.[2]

The cystogram radiograph (Figure 1) shows the tube curved in the dome of the bladder, crossing itself at the bladder neck and its end engaged in the posterior urethra. On withdrawal the tube remained doubled up and became impacted in the urethra in this position, with its lumen obstructed. An excessive length of the tube was introduced into the bladder and became bent with its end reentering the posterior urethra instead of coiling up in the bladder. This rare complication would have been avoided if the introduction of the tube into the bladder had stopped as soon as urine flowed through the catheter indicating that the end of the catheter had entered the cavity of the bladder.

Laboratory Letter

On Borderline Bilirubins

"A man's liver is his carburetor"
Anonymous

If a man's liver is his carburetor, then what he eats and drinks is his fuel mixture and the bilirubin he excretes is part of his exhaust fumes. Vary the mixture, and you vary the fume level.

A far-fetched metaphor? Not really. Consider two conditions that lead to borderline high bilirubins—alcohol ingestion and Gilbert's syndrome. The latter is a harmless familial disorder characterized by a persistent, but variable bilirubin rise often accompanied by vague gastrointestinal complaints.

If you flood your carburetor with alcohol, you're likely to foul your exhaust. Read our study of 500 alcoholics[1], and you'll find 198 of the 500, or nearly 40%, had high bilirubins. But the fumes were rarely pure bilirubin. Only eight patients had isolated high bilirubins; 190 had mixed in the exhaust other elevated abnormal tests—SGOT, alkaline phosphatase, uric acid, LDH, and total protein.

If you have only a borderline bilirubin, then, chances are small alcohol is causing your liver to sputter. The odds are probably greater you have a slightly defective carburetor—congenital hepatic dysfunction, or Gilbert's syndrome.

What is the incidence of this syndrome? Well, at Yale University Hospital, where liver profiles are routine, Levine and Klatskin reviewed 33,560 consecutive charts and found 601 patients with a total bilirubin of 1.5 mg% or greater with a direct fraction of less than 0.3 mg%[2]. Of these 601 patients, the authors classified 366, or one of the original 92, as having "unconjugated hyperbilirubinemia without overt hemolysis", another term for Gilbert's syndrome. This jibes with our experience. Of our last 1280 SMA-12/60 chemistry graphs, 14, or one of 91, had isolated total bilirubins of 1.5 mg% or greater.

So what does Gilbert's syndrome have to do with carburetor? As I mentioned you can think of the liver in the syndrome as a defective carburetor (actually it's probably a deficiency of hepatic glucuronyl transferase). The fuel mix and exhaust are important, too. If you limit the food intake in Gilbert's patients to less than 400 calories a day for 36 to 72 hours, the total bilirubin will abruptly rise two to three-fold, then fall back to its original level within 48 hours when you resume a normal diet[3]. Furthermore, the exhaust product in Gilbert's syndrome is usually pure bilirubin. Almost by definition, SGOT, LDH, and alkaline phosphatase are normal in this disorder.

The moral of the metaphor? If a borderline bilirubin causes you to suspect a congenitally defective carburetor, cut down the fuel and check the exhaust.

Richard L. Reece, M.D.
Minneapolis, Minnesota

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What loneliness is more
lonely than distrust?—George Eliot

Neurological Grand Rounds

Intracranial Abscess

PHYLLIS MELOFF, M.D.*

Localized suppurative lesions within the cranial cavity, which include epidural, subdural, occasionally subarachnoid and brain abscesses, have been recognized at least since 1773 when Richter reported finding pus posterior to an eroded frontal sinus in a 50-year-old man suffering from hemiparesis, aphasia and chronic sinusitis. Since the 1940s, antibiotics have supplemented surgical management of the disease. Yet, despite increasing knowledge of the disease process and improved therapy, difficulty with diagnosis persists, as does high morbidity and mortality. According to a recent review by Garfield[5] mortality is about 40 percent. Other authors[3,4] agree with this figure as an overall mortality rate but suggest that operative mortality, especially since the advent of penicillin therapy, is about 20 percent. However, Liske[7] compared pre-antibiotic and post-antibiotic mortality figures and found no appreciable difference; both were about 60 percent.

A study carried out between 1955-65 at the Minneapolis Veterans Administration Hospital by Gregory[2] indicated that the incidence of the disease did not change over this period. Others[4,5,7] confirm his results. A large urban general hospital may expect to see about five cases of intracranial abscess a year.

Incidence

Intracranial abscesses predominate in the first four decades of life with the highest incidence in the second decade.[3,7] A male preponderance of 2:1 is reported,[3,9] and Heineman[9] mentions an unexpected preponderance of whites, out of keeping with his center's high Negro population (Pittsburgh). Intracranial abscesses are related to infection in other parts of the body except for those which result from head trauma. The sites of original infection have changed little through the year.[3,9,6] Ear and mastoid infections are the most frequent source, followed roughly in order by paranasal sinus infections, metastatic infections from lung and pleura (including lung abscesses, bronchiectasis, emphysema), heart (endocarditis, frequently secondary to congenital heart disease), skin infections (usually of the face), infections following brain surgery and birth trauma. Head trauma and unknown sites each account for 10 percent of the cases.

Bacteriology

Bacteriological findings upon culture of pus obtained at surgery or autopsy from intracranial abscesses show streptococcus, pneumococcus or staphylococcus most often according to Brain[8] and the majority of other authors. Victor[6] notes that subacute bacterial endocarditis of the streptococcus viridans variety is rarely complicated by brain abscess, in contrast to acute bacterial endocarditis caused by staphylococcus aureus, beta hemolytic streptococcus and pneumococcus. The postulated reason for this is immunity of the central

*Neurology Service, Minneapolis Veterans Hospital.

nervous system (CNS) to chronic infection. This is in contrast to Heineman's[9] statement that the majority of abscesses are secondary to a focus of chronic suppuration which he believes accounts for the frequent finding of anaerobes such as bacteroides and streptococcus viridans. Authors reporting a high incidence of sterile cultures may be failing to perform careful anaerobic studies. Loeser[3] compared cases during periods of different therapeutic agents. He found more pneumococcus in the sulfa period from 1940-44, streptococcus viridans in the later 1940s (the penicillin period), and an increasing number of sterile cultures since introduction of broad-spectrum antibiotics. Liske[7] expressed a concern, not shared by others, that the use of antibiotics is creating resistant strains (e.g., streptococcus viridans) responsible for brain abscesses. A host of other organisms have been implicated with abscess formation including coliform bacilli, actinomyces and blastomyces, aspergillus, tuberculosis, cryptococcus, nocardia, coccidioides, candida, etc.

Pathogenesis

The pathogenesis of intracranial abscess is described by Victor[6] and Miller.[10] First, there may be *direct implantation* of organisms due to trauma. Second, there is the possibility of *direct extension* from a site of osteomyelitis (e.g., mastoid, frontal, sphenoidal) followed by local inflammation of dura with adherence to bone and subsequent penetration through meninges into underlying brain substance. Alternatively, this mechanism may give rise to subdural or epidural abscess or meningitis, or a combination of any of these; the factors involved in the choice of form not being understood. Third, and perhaps most frequent, is the process of extension of organisms *along tracts of intracranial veins* and sinuses. Thrombophlebitis of pial veins and dural sinuses block normal blood flow and lead to infarction of brain tissue, thus rendering it more suitable for growth of organisms. The spread along venous channels explains why abscesses are sometimes found far away from the original source of infection. Fourth, infective emboli or heart vegetations as well as septicemia may give rise to metastatic abscesses in an arterial distribution (usually the middle cerebral artery). Multiple abscesses are formed by this process in about 40 percent of cases.

Pathology

Pathologically a division is made by Gregory[2] into micro- and macroabscesses. Histologically, the former show occlusion of small vessels surrounded by clusters of bacteria, necrosis of vessel walls, perivascular infiltration of leukocytes with fibroblastic reaction or destruction of neurons. The latter comprise a gross focal collection of pus with or without a capsule.

Sequence

The sequence of events[6] in gross abscess includes the formation of an inflammatory exudate, mostly leukocytes surrounding blood vessels followed by necrosis of brain with the center of the lesion occupied by a mixture of organisms, necrotic brain and white blood cells, and surrounded by edematous parenchyma, macrophages, glial cells and many small leukocytes (cuffed veins). This is sometimes referred to as cerebritis. The intensity of reaction soon subsides, and a wall of granulation tissue forms around the pus. More chronically collagenous connective tissue replaces granulation tissue, but evidence of infection outside the capsule is

still found. In addition, the capsule is known to be of varying thickness. It is possible for encapsulated abscesses to continue invasion into white matter and become multilocular or rupture into the ventricles with catastrophic results.

Location

Abscesses can localize anywhere in the brain, but they predominate in the frontal and temporal lobes.[2,5] Parietal and subdural foci are also common and multiple foci vary from 5 to 48 percent in different studies.[4,5,7] In general, mastoid infections lead to abscesses in the middle cerebrum, temporal lobe or cerebellum (more commonly in children than adults by 3:2); sinus infections lead to abscesses in the anterior cerebrum, and metastatic abscesses often localize in the distribution of the middle cerebral artery. Basal ganglia, thalamus and brain stem are rare sites for gross abscesses, although microabscesses were not uncommon in these sites in Gregory's[2] study.

The incubation period for the disease in Loeser's[3] study was less than two months in over 50 percent, from two months to one year in 15 percent, and from six months to 20 years in 25 percent of cases.

Clinical Manifestations

Symptoms

Symptoms vary depending upon the location of the abscess. The most frequent symptom described is headache[2,6,10] often unilateral; followed in rough order of frequency by fever, drowsiness, confusion, personality change, focal seizures, nausea and vomiting, focal motor, sensory and speech disorders.

Signs

According to Loeser,[3] neurological signs on initial examination ranked in order of frequency as fellows: hemiparesis, hemiplegia, central facial palsy—60 percent; papilledema—50 percent; aphasia—25 percent; convulsions—20 percent; hemisensory deficit—18 percent. Cerebellar and Parkinsonian signs were far less frequent. Other physical signs included: ear infection and tender sinus—30 percent; heart murmur, cyanosis, clubbing—30 percent; temperature—40 percent (one-half had signs of meningitis); pulse 60—10 percent due to increased intracranial pressure.

Laboratory Tests

White blood count was elevated in 70 percent, sedimentation rate was increased in 80 percent. The spinal fluid showed 20 to 99 cells or less than five cells in the majority of cases. The protein was elevated. Sugar was not usually diminished unless suppurative meningitis coexisted. Organisms were absent except with concomitant meningitis.

Roentgenologic Studies

Xrays revealed a normal skull series in 50 percent. Others showed increased intracranial pressure. Sinus xrays revealed infection in 20 percent.

Contrast procedures were of localizing value as follows: ventriculogram localized the lesion in 50 to 84 percent; arteriogram localized the lesion in 10 to 73 percent; and pneumoencephalogram localized the lesion in 3 to 5 percent.

The arteriogram may be of value in distinguishing epidural and subdural

abscesses from each other and from brain abscesses. The former two initially resemble hematoma in early stages with downward displacement of cortical arteries, veins and sinuses. The brain scan, although not widely used in the studies heretofore reported, have proved of considerable localizing value.[2]

The electroencephalogram is valuable in localizing up to 60 percent of abscesses and characteristically shows focal delta activity in the involved area.

Differential Diagnosis

Intracranial abscesses usually run a rapid, progressive course but may be slow and mimic neoplasm. The differential diagnosis includes meningitis, cerebral thrombophlebitis, acute necrotizing hemorrhagic encephalopathy, primary and metastatic neoplasms, especially metastatic meningeal carcinomatosis, and massive ischemic infarction.[6,10] Some points in differential diagnosis include: high remittent fever in thrombophlebitis and subdural abscess, more frequent bradycardia with subdural abscess, focal signs more common in brain abscesses than in meningitis, with the reverse being true of meningeal signs, tenderness to palpation over affected area with extradural abscess, less frequent headaches with cerebral infarcts, slower progression of symptoms in tumors, and red cells in the cerebrospinal fluid with acute necrotizing hemorrhagic encephalopathy. A careful history is the most important diagnostic aid although present day antibiotic treatment for original sources of infection may delay the onset of symptoms of abscess from the initial infection, making diagnosis difficult.

Therapy

Therapy for intracranial abscesses is ultimately surgical with the exception of extradural abscess which may at times respond successfully to antibiotics alone.[10] Surgical therapy includes aspiration, drainage, packing and excision. Miller[10] pointed out that multiple abscesses may be missed on aspiration. On the other hand, excision carries the hazard of adding to the neurologic deficit as noted by Jooma and Pennybacker.[4] In general, excision is thought to carry a lesser mortality than aspiration, about 20 percent compared to 40 percent. Loeser[3] reports a 22 percent mortality with aspiration plus a combination of penicillin, sulfa and broadspectrum antibiotics as compared to 41 percent with aspiration and sulfa alone. Jooma[4] reports a 27 percent mortality with penicillin and 53 percent without penicillin. The site of abscess has little influence on mortality figures. Apart from danger to life, sequelae of abscesses include hemiparesis, aphasia, seizures (most commonly) and recurrence of abscess, which occurred in eight percent of Jooma's cases treated with aspiration or drainage.

Early Procedures

Garfield[5] suggests that the following course of management will lower mortality. As soon as a diagnosis of brain abscess is suspected, the patient should be transferred to a neurosurgical ward but lumbar puncture should not be performed because of the real risk of herniation owing to increased intracranial pressure.

Patients should be started on 4 million units of penicillin every six hours. Xrays of skull and chest and thorough otolaryngological exploration should be done. An electroencephalogram is of value if the patient's condition permits and time allows.

The State of Consciousness

Fully alert patients should continue on penicillin and have a brain scan within 48 hours. If the scan is negative, patients should be treated expectantly with antibiotics. Drowsy patients should receive penicillin and Mannitol (or Decadron) and have a brain scan within 24 hours. If a brain scan cannot be done and the site of obvious ear-nose-throat sepsis is found, appropriate burr-hole with aspiration should be performed. Thorotrast or pantopaque may be instilled into the abscess cavity so that the shrinkage may be followed radiographically. Angiography or a ventriculogram is indicated to identify the site of an acute non-encapsulated abscess. Unconscious patients should have penicillin and immediate Mannitol (or Decadron) and burr-hole with aspiration for obvious ear-nose-throat sepsis. A delay of up to three hours for brain scan is justifiable, but if it cannot be done in that time, a ventriculogram should be performed instead.

Conclusion

Garfield[5] emphasizes the haste required in diagnosis and treatment of this condition and places less emphasis on the specific surgical method as being decisive in determining the outcome.

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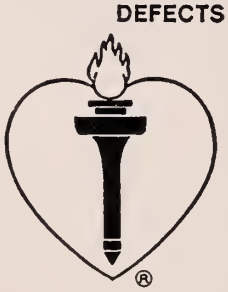
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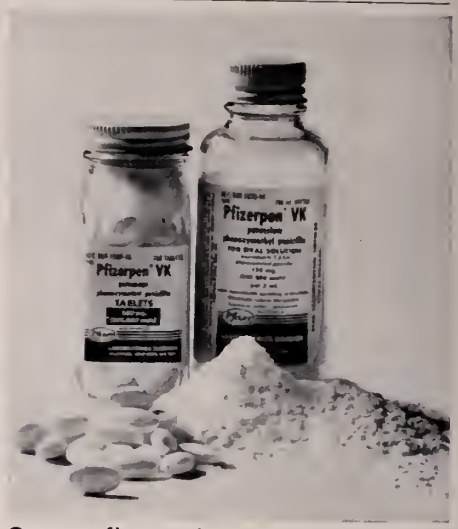
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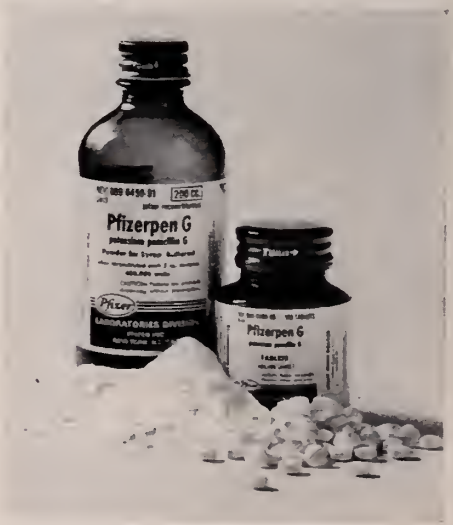
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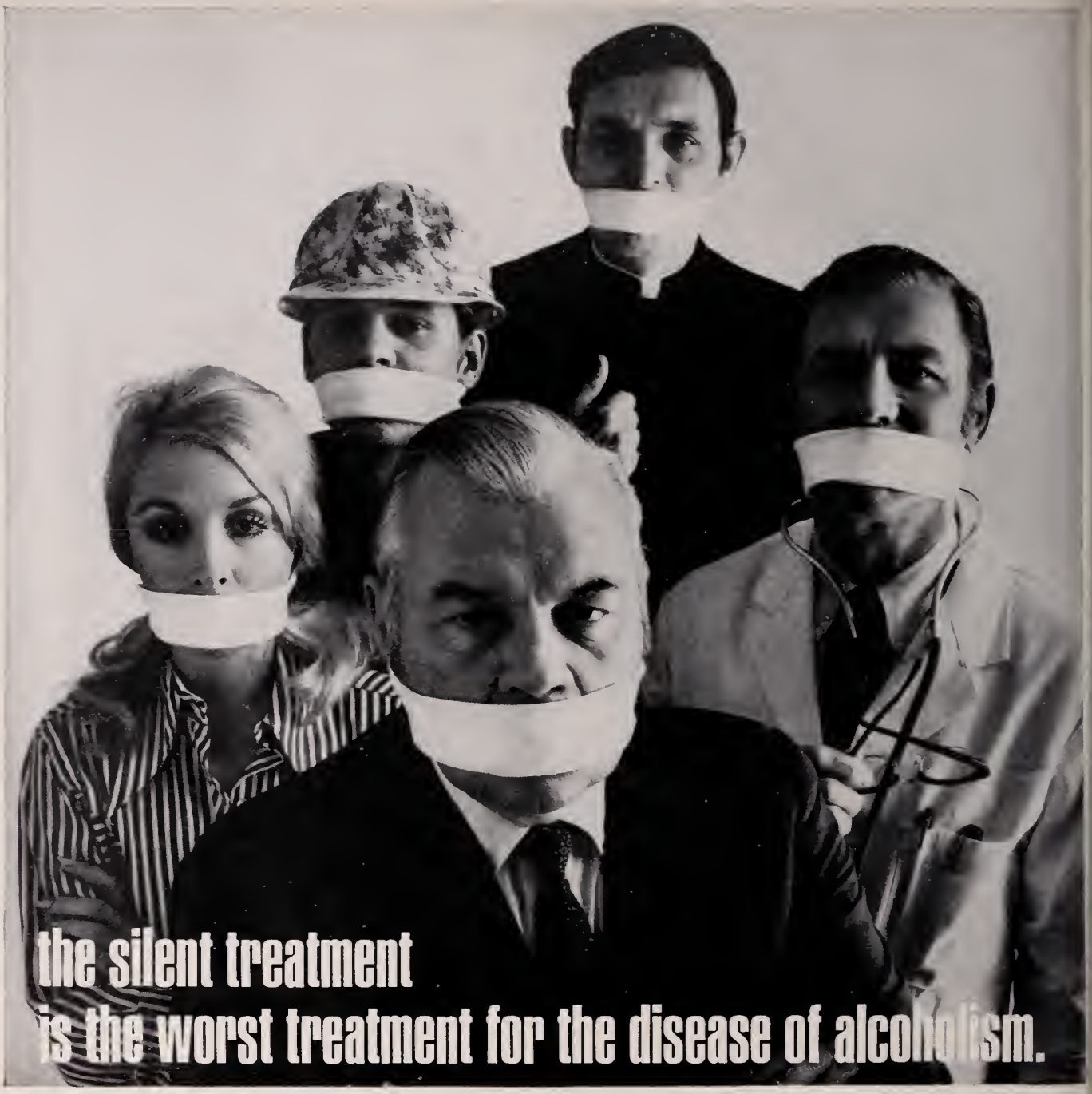
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- Blood pressure above 140/90 is accompanied by increased morbidity and requires close medical attention.
- Even small increments in either systolic or diastolic blood pressure progressively and steeply shorten life expectancy.

Other Studies. Studies conducted with large numbers of patients since that time have echoed the above findings. Two studies published in 1970—the VA Cooperative Study Group on "Effects of Treatment on Morbidity in Hypertension"[2] and the "Framingham Study"[3]—suggest that treatment of even mild hypertension may, over time, offer significant benefits to the patient.

Another Point of View. Although a growing body of studies suggests that treatment of mild hypertension is warranted, medical opinion is not unanimous. Some clinicians recommend that drug treatment for mild hypertension be reserved for patients with additional risk factors such as smoking, high cholesterol levels, heart or kidney involvement, or a family history of vascular disease. Dr. Walter M. Kirkendall stated this position in his recent paper "What's With Hypertension These Days?"[4] Discussing the management of hypertension in patients with a sustained diastolic pressure up to 100 mm Hg, he said: "Generally, I do not recommend antihypertensive therapy unless patient's blood pressure approaches the upper limit for the group and a number of adverse factors exist, such as male sex, family history of vascular disease, youth, evidence of heart or kidney involvement."



Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

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CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to this compound. Nursing mothers; if use of drug is deemed essential, patient should stop nursing.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function to avoid cumulative or toxic effects. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis.

When used with other antihypertensive drugs, careful observation for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents, especially ganglion blockers, must be reduced by at least 50% because HydroDIURIL potentiates their action.

Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery was frequently required, and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs.

Thiazides cross placenta and appear in cord blood. In women of childbearing age, potential benefits must be weighed against possible hazards to fetus, such as fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives, including thiazides.

PRECAUTIONS: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive or patient is receiving parenteral fluids. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop (especially with brisk diuresis) in severe cirrhosis; with concomitant steroid or ACTH therapy; or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypokalemia may be avoided o treated by use of potassium chloride or giving food with a high potassium content. Similarly, any chlorid deficit may be corrected by use of ammonium chlorid (except in patients with hepatic disease) and largel prevented by a near normal salt intake. Hypochloremi alkalosis occurs infrequently and is rarely severe. I severely edematous patients with congestive failure o renal disease, a low salt syndrome may occur if dietar salt is unduly restricted, especially during hot weathe

Thiazides may increase responsiveness to tubocu rarine. The antihypertensive effect of the drug may b enhanced in the postsympathectomy patient. Arteri responsiveness to norepinephrine is decreased, neces sitating care in surgical patients. Discontinue drug 4 hours before elective surgery. Orthostatic hypotensio may occur and may be potentiated by alcohol, barbi urates, or narcotics.

Pathological changes in the parathyroid glands wit hypercalcemia and hypophosphatemia have been see in a few patients on prolonged thiazide therapy. Th effect of discontinuing thiazide therapy on serum ca cium and phosphorus levels may be helpful in asses ing the need for parathyroid surgery in such patient Parathyroidectomy has elicited subjective clinical im provement in most patients, but has no effect c hypertension. Thiazide therapy may be resumed aft surgery.

Use cautiously in hyperuricemic or gouty patient gout may be precipitated. May affect insulin requir ments in diabetics; may induce hyperglycemia ar glycosuria in latent diabetics.

ADVERSE REACTIONS: Rare reactions inclu thrombocytopenia, leukopenia, agranulocytosis, apla tic anemia, cholestasis, and pericholangiolitic hepatit Nausea, vomiting, diarrhea, dizziness, vertigo, pare thesias, transient blurred vision, sialadenitis, purpu rash, urticaria, photosensitivity, or other hypersen tivity reactions may occur. Cutaneous vasculitis p cipitated by thiazide diuretics has been reported elderly patients on repeated and continuing exposu to several drugs. Scattered reports have link thiazides to pancreatitis, xanthopsia, neonatal thro bocytopenia, and neonatal jaundice. When adve reactions are moderate or severe, the dosage thiazides should be reduced or therapy withdrav

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Perinatal

The Perinatal Care Center

MARTHA J. BURKE-STRICKLAND, M.D. and DONALD W. FREEMAN, M.D.

WIDESPREAD INTEREST is beginning to develop in perinatal care centers whose broad purpose is to improve perinatal care.[1,2,3] These centers involve the combined efforts of physicians and other health workers concerned particularly with obstetrics, pediatrics and anesthesia. Ideal care of the sick newborn begins before his birth with recognition of a high-risk situation in pregnancy. Intensive care during the remainder of that pregnancy and during labor and delivery and the uninterrupted continuation of special care in the newborn intensive care unit should be followed by health-maintenance care until the needs of both the mother and the infant can be met by other community facilities. Perinatal centers are designed to provide such care.

The development of such a perinatal center at HCGH started when a high-risk problem obstetrics outpatient clinic began functioning at Hennepin County General Hospital (HCGH) four years ago. Amnioscopy and fetal blood sampling techniques for detecting fetal distress were introduced about the same time. In 1969, the obstetrical service began exploring electronic monitoring of the fetal heart rate and intrauterine pressures. Concomitantly the pediatric service began putting together a newborn intensive care unit (NICU). The follow-up high risk infant clinic was opened in 1970.

Mutual discussion and review at biweekly meetings of the obstetric, pediatric and often the anesthesia staffs have brought increasing awareness of problems as well as solutions to some of the problems. This interdepartmental cooperation has been the focal point in the translation of the perinatal care center concept into a functioning continuum of service at HCGH.

Since HCGH serves a population with an increased incidence of high-risk pregnancies and as a teaching hospital has the reservoir of skilled personnel necessary to staff such a program, it is appropriate that HCGH should be one of the pioneers of this approach in the State of Minnesota. Since these changes do carry a price tag and come at a time when all medical costs are under critical scrutiny, it is reasonable to ask: Does the program make any real difference?

Comparing earlier statistics of the program with later phases suggests that the entire program is beginning to have significant measurable results. For example the total perinatal mortality rate decreased from 45 per 1,000 live births in 1969, to 23.6 in 1971. The percentage of patients with high-risk situations remains high and has been generally without significant change in the three year period. Fourteen percent of the babies born at HCGH are in the low birth weight category (500-2,500 grams), premature rupture of membranes occurs in 16%, hypertensive toxemia in 8% and intravenous oxytocin is needed for induction of labor or treatment of abnormal labor patterns in 17%.

Since the pathogenesis of neonatal Respiratory Distress Syndrome (RDS) appears to be related to hypoxic stress of the fetus and the newborn, the incidence and survival of newborns with RDS

TABLE
Data From Hennepin County General Hospital Perinatal Care Program

	1969	1970	1971
Fetal Death Rate*	16.2	14.0	10.5
Newborn Death Rate*	29	16.2	13.2
Perinatal Death Rate*	45	30.5	23.6
Prematurity Rate	14.5%	15.2%	13 %
Premature Death Rate*	18.4%	11 %	9.2%
Incidence of RDS*	(36.5)†	36	21
Survival of RDS	(46 %)†	70 %	56 %

* Per 1,000 live births at HCGH.
† Close estimate; uniformity in recording data not established.

may be used as another indicator of the effectiveness of management of the newborn.[4] Monitoring the fetus during labor and delivery permits manipulative intervention on behalf of the fetus as well as anticipatory treatment of shock when present in the infant at birth. During the last half of 1971, such monitoring became feasible for nearly all the labors that needed it. Seventeen percent of all labors are now electronically monitored. The pediatric team is alerted whenever signs of stress are detected in the fetus and is on hand in the delivery room to assist in care of the baby. With no change in criteria for making the diagnosis, the incidence of RDS among babies born at HCGH dropped from 36 per 1,000 live births in 1969 and 1970, to 21 per 1,000 live births in 1971.

The survival rate of infants with RDS decreased to 56% in 1971, after a very satisfactory 70% survival in 1970. Analysis of contributing factors gives hope for a better future and a cogent argument for the idea that an intensive care unit must be properly staffed and equipped if it is to make a difference.

As the newborn intensive care service developed at HCGH, the demands rapidly exceeded the capacity of the unit. During the first few months of 1971, the unit operated in temporary makeshift quarters. An appalling death rate in the unit during January and February made it clear that it was no favor to anyone to operate in such a fashion. Time studies confirmed the staff-patient ratios needed to render different levels of care in the unit. It was agreed to follow established guidelines even if some babies born at HCGH had to be transferred to other special care units. This would permit the staff to give real intensive care. The difference in RDS mortality during the two periods of 1971 is striking. Eight of ten cases died during January and February with a survival of only 20%. The figures reversed for the rest of the year with a survival of 70%. The eight deaths of 27 cases in that period included one infant who was transferred and died in another unit.

To this point only numbers salvaged have been presented. Assessment of the quality of life thus preserved is more difficult. Accumulation of long-term data on many variables is needed for definitive answers; however, preliminary reports are encouraging. For example, though the percentage of babies delivered by cesarean section who come to the NICU has not changed significantly, the average length of stay in the unit has decreased from 15.5 days to eight days. Of 29 infants who required respirator assistance for survival and who have been followed for at least eight months after discharge from the unit, only five, or 17%, have severe neurological handicaps. This means that 24 infants who would not have survived at all in the traditional care setting have survived with intensive care as reasonably intact individuals who should be able to function effectively in society. In all 17 infants who have survived oxygen therapy with residual bronchopulmonary dysplasia, x-ray follow-up for six to 18 months showed that gradual architectural restoration of the lung is occurring. The incidence of recurrent pulmonary infections requiring rehospitalization for these infants has been reduced by instituting a home program of nebulization and physiotherapy.

An improved system for data collection and retrieval is underway for 1972. This should provide more of the long-term answers desired as well as help to focus attention on areas that need improvement. In the meantime, indications seem to be that coordinated intensive perinatal care does make a difference at HCGH.

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Reminder

119th Annual Meeting of the Minnesota State Medical Association in Rochester, Minnesota, May 18, 19 and 20, 1972.

Review

Laparoscopic Sterilization

STEPHEN L. LARSON, M.D.*

USE OF THE LAPAROSCOPE for female sterilization has gained favor in recent years. The procedure was first suggested by Anderson[1] and by Power and Barnes[2] about thirty years ago. However, Palmer[3] of France, Steptoe[4] of Britain and Frangenheim[5] of Germany first performed such sterilizations in the early 1960's. Within the last four years, many American investigators have found the procedure useful.

Technique

The procedure of laparoscopy is performed in the usual fashion.[3] Usually no preoperative enema, catheterization or shaving is required. The operation can be done on the day of admission to the hospital. In brief, the tubal sterilization is accomplished as follows. Under laparoscopic control, the isthmic area of the uterine tube is grasped with a tong, biopsy forceps or grasping forceps. When a moderate coagulation current is applied, the tube can be seen to blanch in a radial fashion for 1 to 2 cm. in either direction and into the mesosalpinx. The operator often will feel a popping sensation as the isthmic region is coagulated. Some authors[6,7,8,9] advocate that the tubes not be transected to prevent tubal fistulae. However, others describe division of the tube through the coagulated area, with or without removal of a segment for biopsy. This is accomplished with ease and with no bleeding. With rare exception, the patient may be discharged within 24 hours after surgery.

Outpatient sterilization using the laparoscope has been employed to reduce hospitalization and procedure costs. The patient is admitted the morning of surgery, after fasting. Wheeless[10] was able to discharge 73 of 75 patients at eight hours after surgery. There were no postoperative complications in this group. Steptoe frequently discharged his patients after nine hours.[11] Peterson and Behrman[12] believe that patients can be safely discharged eight hours after laparoscopy if the vital signs were stable. If bleeding occurs, it is found at operation or in the immediate postoperative period. Suction curettage for induced abortion, in combination with laparoscopic sterilization, may be done on an outpatient basis.[13]

Postoperative Hysterosalpingography

Opinions differ regarding the role of postoperative hysterosalpingograms. Liston et al.[7] found the procedure useful and discovered two failures and two tuboperitoneal fistulae among 78 patients having hysterograms. They, therefore, recommend tubal electrocoagulation without transection as the sterilization procedure of choice. Wheeless[14] used hysterosalpingography to identify the patients with fistula for possible reoperation. Peterson and Behrman[12] abandoned the procedure for fear that the hydrostatic pressure applied would open the medial stump on the transected tube and thereby favor future ectopic or uterine pregnancy. Steptoe[15] has also discarded this procedure because the only two pregnancies among 1350 patients followed salpingograms that produced fistulae. Other authors described cases in which flow of the radiopaque dye from the medial end of a transected tube was observed, but subsequent laparoscopy demonstrated tubal occlusion.[7,16] Jordan et al.[9] demonstrated that methylene blue injection at the time of operation was of no value, because postoperative fibrosis is necessary for the desired effect of tubal occlusion. Their hysterosalpingograms showed this process to be incomplete at six weeks. By 12 to 16 weeks after sterilization, fibrosis was complete. In summary, follow-up hysterosalpingography is useful to detect tuboperitoneal fistulae or technical failure (cautery of the round ligament or of the utero-ovarian ligament) but there probably is a substantial risk of the procedure forcing open the sealed medial end of the uterine tube.

Combined With Induced Abortion

In some instances therapeutic abortion has been performed at the time of laparoscopic sterilization. Steptoe and Imran[13] described 101 such cases with an average postoperative hospitaliza-

*Minneapolis, Minnesota.

tion of 2.4 days. Some, however, returned home nine hours after surgery. At the time of laparoscopy, they inspected the uterus for effective contractions and for possible perforation. They emphasized great care in handling the uterine tubes during pregnancy to avoid traumatic bleeding. One of these patients underwent laparotomy for bleeding, another developed a pelvic abscess and required antibiotics for a low grade fever. Steptoe's total series of combined operations has been increased to 189.[15] Fifty-six additional instances of the combined procedure have been noted in the literature.[7,8,12,17]

Postpartum

Keith et al.[18] have found sterilization by laparoscopy to be useful in the postpartum period. The procedure was done as late as the sixth postpartum day among 44 patients. Uterine trauma occurred in "several" patients from the instrumentation. In addition, three patients were explored (one for bleeding), one patient herniated omentum through the abdominal incision, and nine patients experienced anesthetic complications. Steptoe has used this technique in 61 patients without problem.[15] Siegler[19] has stated that this method is not the procedure of choice for postpartum tubal ligation, and other authors[20] believe that it does not compete with the standard technique of postpartum sterilization. The lack of reported cases of this variation of laparoscopic sterilization may indicate its lack of popularity.

Failures

Pregnancies that follow laparoscopic sterilization must be divided into operator failures and procedure failures of nine pregnancies reported after 760 sterilizations by Liston,[7] five patients were in the luteal phase of the cycle at the time of laparoscopy and were unknowingly pregnant. One of these patients maintained the pregnancy despite a curettage at laparoscopy. Two others had electrocoagulation of the round ligament and, in another patient, "the operator seemed to have omitted to deal with one appendage." The ninth patient was a true procedure failure with an ectopic pregnancy after tubal diathermy and division, verified by hysterosalpingogram and proved at laparotomy. Eight authors reported a total of 3,658 laparoscopic sterilizations with five true failures (Table). These failures may be compared to the overall failure rate of 1 in 140 procedures, calculated by Garb[21] from 30,000 tubal ligations reported in 46 articles. Among 5,477 Pomeroy procedures, he found that one in 250 had failed.

Restoration of fertility is theoretically possible after laparoscopic sterilization.[20] Donald[22] uses a scissor technique for tubal transection without biopsy and the utero-ovarian arterial anastomosis is not incised. The distal portion of the tube may be reimplanted at a later date. There are no reports of a successful reimplantation.

Complications

Complications of the procedure are infrequent. None have been reported among 108 procedures by three authors.[16,17,23] The larger series of sterilized patients have required laparotomy in about one of 200 procedures. Nine authors with fifty or more patients and with complications stated had a total of 3,702 procedures. Sixteen patients had laparotomy for bleeding that could not be stopped under laparoscopic control. In a preliminary report from Johns Hopkins[24] eight of 800 patients were explored, most of them for bleeding. Because the majority of the complications occurred with the first 200 patients, lack of experience may play an important role. The tearing or shearing action of the tong may con-

TABLE

Author	Number of Patients	Tubal Sterilization Done But Failed	Tube Not Sterilized (Operator's Mistake)	Patient Pregnant at Operation
Chun[20]	120	0	1	1
Cohen[16]	50	0	0	0
Corson[26]	57	0	0	0
DeBoer[27]	150	1	1	0
Jordan[9]	910	0	1	3
Liston[7]	760	1	3	5
Peterson[12]	186	1*	0	0
Steptoe[15]	1350	2	0	0
Wheeless[10]	75	0	0	0
TOTAL	3658	5	6	9

*Incomplete tubal transection found at laparotomy.

tribute to bleeding from the mesosalpinx,[12,25] if the operator does not use the cutting current effectively.

The following complications have been directly related to the sterilization. Salpingitis has been noted.[8] One patient was found to have a tubo-ovarian abscess four weeks after surgery.[14] Another patient required drainage of a pelvic abscess after therapeutic abortion and laparoscopic sterilization.[13] The serosa of the colon has been electrocoagulated on one occasion without complication.[12] Twice the small bowel has been coagulated, leading to resection in both instances.[9] Other reported complications related to the laparoscopy are perforation of the stomach[12] or the bowel,[9,20,24] postoperative pneumonia,[10] herniation of the omentum through the umbilical incision,[18] and anesthesia problems.[18] The overall percentage of significant problems, however, remains acceptably low. In the large combined experience of Palmer and Steptoe, it has been said that no significant complications have occurred.[23]

In our practice, 135 laparoscopies have been performed. Approximately 25% of these patients had previous abdominal surgery; on no occasion did this prohibit performance of the intended operation. Sixty-seven patients had laparoscopic sterilization, several of these patients requesting tubal severance at the same time as curettage for abnormal bleeding or laparoscopy for diagnosis of pelvic pain. There have been no instances of febrile morbidity, abscesses, hematomas, or pregnancy. One patient required immediate laparotomy to achieve hemostasis in the mesosalpinx. The patients generally remained in the hospital 24 hours after the procedure, and returned to full activity in two to seven days. Vaginal tubal sterilization recently has been reported to have complication rates of 9.6%[28] and 2.4%.[29] Our preliminary series would seem to compare favorably with these figures.

Summary

Improved methods of family limitation must be discovered to meet ever increasing demands by fertile couples. Male sterilization is a simple and effective procedure with low morbidity and has achieved popularity. For some couples, however, the woman must be the one to undergo a surgical procedure for termination of fertility. Laparoscopic sterilization is a rapid method associated with low morbidity and minimal hospitalization. Patients may make use of these advantages without sacrificing effectiveness.

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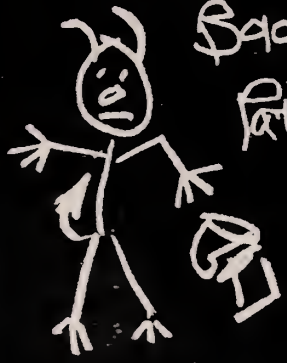


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Willie Warner

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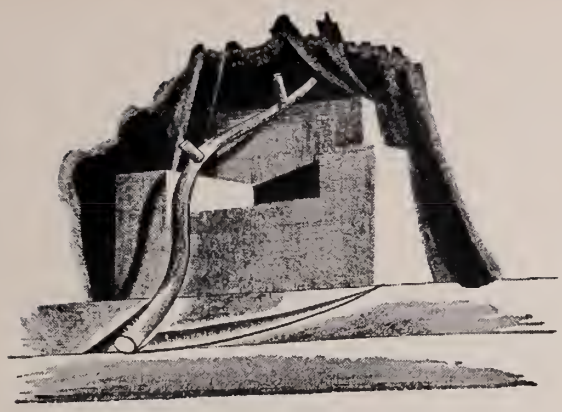
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In Memoriam

Lovely in death the beauteous ruin lay.

RALPH B. JOHNSON, M.D.

Dr. Ralph B. Johnson, Lanesboro physician, died September 4. Born in LaCrosse, Wisconsin, Dr. Johnson attended the Northwestern University Medical School.

He was a member of the Olmsted, Houston, Fillmore and Dodge County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Edna, and two children.

BURTON C. FORD, M.D.

Dr. Burton C. Ford, 80, Marshall physician died October 17. Born in Winona, Minnesota, Dr. Ford received his medical education at the University of Minnesota.

He was a member of the Lyon-Lincoln Medical Society, the Minnesota State Medical Association and the American Medical Association, and was a former member of the State Board of Nursing Examiners.

Dr. Ford is survived by his wife, Loretta, and four children.

JOSEPH C. MICHAEL, M.D.

Dr. Joseph C. Michael, 82, Minneapolis neurologist, died September 2. A native of Jordan, Dr. Michael was a graduate of the University of Minnesota Medical School and did postgraduate work in France and Austria.

He was a former clinical professor at the University of Minnesota and a former chief of staff of the neuro-psychiatric department at Hennepin County General Hospital. He was a member of the American Board of Psychiatry and Neurology, Hennepin County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association. Dr. Michael was also a former staff member of various local general and private hospitals.

Dr. Michael is survived by his wife, Blanche, and a son, Joseph, Jr.

NELS G. MORTENSEN, M.D.

Dr. Nels G. Mortensen, 87, died October 23. He had been a physician and surgeon in St. Paul for 35 years. His medical education was obtained at the University of Minnesota Medical School.

He had been president of the State Board of Health for 15 years, past Grand Chef de Gare of the Minnesota 40 & 8, a past president, 50 Club and Life member of the Minnesota State Medical Association, and a member of the American Medical Association and the Park Region Medical Society.

Dr. Mortensen is survived by his wife, Violet.

EARL J. BLACK, M.D.

Dr. Earl J. Black, 67, died February 10. Born in Bemidji, Dr. Black was a St. Paul area resident 39 years, and had been in private practice here following service with the Army in World War II.

He was a member of the American Medical Association and the Ramsey County Medical Society and an Associate Member of the Minnesota State Medical Association.

Dr. Black is survived by his wife, Ramona, a son, Anthony, and two daughters, Sara and Susan.

HELEN L. HABERER, M.D.

Dr. Helen L. Haberer, 65, head of the Department of Gynecology at the University of Minnesota Health Service, died February 1. She had been a member of the staff at the health service since 1952 and had directed the gynecology department since 1958.

She was born in Fergus Falls, Minnesota and received her medical degree from the University of Minnesota.

Dr. Haberer was a member of the American Medical Association, the Minnesota State Medical Association and the Hennepin County Medical Society.

SIMON G. SAX, M.D.

Dr. Simon G. Sax, 64, internist, died January 5. A native of Eveleth, he was a graduate of the University of Minnesota Medical School. He began his practice in Duluth in 1936 and had lived there since.

Dr. Sax was a member of the American Medical Association, Minnesota State Medical Association and the St. Louis County Medical Society. He was also a member of the Minnesota Academy of Science and the Minnesota Medical Foundation.

Dr. Sax is survived by his two brothers, Dr. Milton Sax and Jonathan G. Sax.

HARLAN A. ALEXANDER, M.D.

Dr. Harlan Alexander, 65, surgeon, died November 19. Born in Minneapolis, Dr. Alexander attended the University of Minnesota Medical School.

He was a member of the American Medical Association, Minnesota State Medical Association and the Hennepin County Medical Society.

Dr. Alexander is survived by his wife, Esther, and two sons, Doctors Harlan G. Alexander and David Alexander.

HENRY V. HANSON, M.D.

Dr. Henry V. Hanson, 82, of Green Valley, Arizona, died October 12. Born in Hutchinson, Minnesota, Dr. Hanson studied medicine at the University of Illinois, graduating in 1912. After serving in the military service, he practiced as an ENT specialist in Willmar. In 1923 he joined the staff of the Veterans' Bureau.

He was a diplomat of the American Academy of Ophthalmology and Otolaryngology, a former Assistant Clinical Professor of Otolaryngology at the University of Minnesota, a member of the American Medical Association and the Hennepin County Medical Society, and a 50 Club and Associate Member of the Minnesota State Medical Association.

Dr. Hanson is survived by his wife, Ethel, and a daughter, Evelynne.

ERNEST R. STERNER, M.D.

Dr. Ernest Sterner, 65, a surgeon practicing in St. Paul, died December 29. Born in Cambridge, Minnesota, his medical education was obtained at the University of Minnesota Medical School.

Dr. Sterner was a former Health Officer of Birchwood, former Ramsey County deputy coroner, and a member of the American Medical Association, Minnesota State Medical Association and the Ramsey County Medical Society.

He is survived by his wife, Virginia, and a daughter, Diana, two of his brothers, Dr. Donald Sterner and Dr. Otis Sterner, practice medicine in St. Paul.

DAVID J. VAIL, M.D.

Dr. David J. Vail, director of medical services for the Minnesota Department of Public Welfare for the last 11 years, died October 21. A native of Cincinnati, Ohio, Dr. Vail received his M.D. degree from Harvard University in 1948. A psychiatrist, Dr. Vail, as medical director, was in charge of the state mental health system, including 10 major institutions for the mentally ill and retarded and statewide networks of community mental health and day activity centers. One of his key accomplishments in Minnesota was initiation of an effort to remove "dehumanization" from state hospitals. He established humane practices committees at state institutions to review both major and minor complaints from patients.

Dr. Vail was a member of the American Medical Association, the Minnesota State Medical Association and the Ramsey County Medical Society.

He is survived by his wife, Joane, four sons, and three daughters.

REUBEN ERICKSON, M.D.

Dr. Reuben Erickson, 75, obstetrician and gynecologist, died December 31. Born in Scandia, Minnesota, Dr. Erickson obtained his degree from the University of Minnesota Medical School.

He was a member of the American Medical Association and the Hennepin County Medical Society and a Life Member of the Minnesota State Medical Association.

Dr. Erickson is survived by his wife, Hazel, daughter, Patricia, and son, Dr. Hartley John Erickson.

CHARLES MICHAEL JESSICO, M.D.

Dr. Charles Michael Jessico, 63, a physician specializing in neurology and psychiatry, died February 17. He had been associated with the Duluth Clinic for 26 years. His medical education was obtained at Loyola University, School of Medicine, in Chicago.

He was a member of the American Medical Association, the Minnesota State Medical Association, and the St. Louis County Medical Society.

Dr. Jessico is survived by his wife, Avanelle, and two sons, Charles and Ronald.

JOHN W. SCHUT, M.D.

Dr. John W. Schut, 51, Anoka physician and specialist in neurology, died February 17, of the disease he had spent nearly all of the latter part of his life studying. He was one of the founders of the National Ataxia Foundation, set up to combat the mysterious disease.

His medical degree was obtained from the Northwestern University Medical School, and he was a member of the American Medical Association, the East Central Medical Society, and an Associate Member of the Minnesota State Medical Association.

Dr. Schut is survived by his wife, Mary.

HENRY S. BLOCH, M.D.

Dr. Henry S. Bloch, 55, internist, died January 10. Born in Munich, Germany, Dr. Bloch's medical education, however, was obtained at the University of Minnesota Medical School.

He was a clinical instructor in the Department of Medicine, University of Minnesota and a member of the American Medical Association, Minnesota State Medical Association, and the Hennepin County Medical Society.

Dr. Bloch is survived by his wife, Maxene.

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one million doses of Mylanta
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Relieves G.I. gas distress*
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a new outlook in chronic pain

of moderate to severe intensity

Though Talwin® can be compared to codeine in analgesic efficacy, it is not a narcotic. So patients receiving Talwin for prolonged periods face fewer of the consequences you've come to expect with narcotic analgesics. And that, in the long run, can mean a better outlook for your chronic-pain patient.

Talwin Tablets are:

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- **Not subject to narcotic controls:** convenient to prescribe—day or night—even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See last page of this advertisement for a complete discussion of adverse reactions and a brief discussion of other Prescribing Information.)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®) may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

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the long-range analgesic

Minnesota State Medical Association

It's All Set for You in '72

119th Annual Meeting

ROCHESTER WILL be the host city for the 119th Annual Meeting of the Minnesota State Medical Association May 18, 19 and 20. Members of the Zumbro Valley Medical Society will be the hosts for the 1972 Upper Midwest's Great Medical Meeting.

In its continued effort to introduce innovations for the meeting, the Committee on Scientific Assembly has approved a program format which will include three concurrent morning sessions for Thursday and Friday. Each session will feature eight mini-sessions 10, 15 or 20 minutes in length.

Afternoon sessions for both days will each feature a series of five "in depth" concurrent panels and roundtables.

Morning sessions will begin at 9:00 A.M. in North Hall, South Hall and the Theater Section of Mayo Civic Auditorium.

The afternoon panels will begin at 2:00 P.M. and will also be held in the Mayo Civic Auditorium locations.

The meeting will feature outstanding scientific and technical exhibits. Recess breaks between sessions have been scheduled at 10:15 A.M. and 3:00 P.M. to give physicians the opportunity to view the exhibits.

Specialty Societies Participate

A number of specialty societies have scheduled annual meetings in conjunction with the 119th Annual Meeting, including the following: Minnesota Society of Clinical Pathologists—May 20; Minnesota Academy of Ophthalmology & Otolaryngology—May 19; Minnesota Chapter of American Academy of Pediatrics—May 19; Minnesota Physiatric Society—May 19; Minnesota Chapter of the American College of Surgeons—May 19 and the Minnesota Chapter of the Flying Physicians Association—May 20.

The Minnesota Chapter of the American College of Surgeons will again sponsor the Friday (May 19) morning program. The Committee on Alcoholism and Drug Abuse will sponsor a presentation titled "The Recognition and Management of the Dependent Person" May 18. The Committee on Environmental Health will sponsor a panel Friday, May 19.

"Something for Everyone"

There will be nearly 100 participants in the 48 mini-sessions, 16 panels and luncheons of the Scientific Program. The Committee on Scientific Assembly is pleased to announce a program which will include a wide range of pertinent and stimulating subjects. Included in the Thursday afternoon panels will be one titled "Meet the Medical School Deans." With the expansion of medical school facilities in Minnesota, this occasion will provide physicians the opportunity to learn more about what's in store for Minnesota. Participants include: H. Drew Miller, M.D., Chairman; Panel Members: Robert E. Carter, M.D., Ward S. Fowler, M.D., and Mead Cavert, M.D. Synopsis of some of the papers scheduled for presentation are listed at the end of this article.

Luncheon Speakers Named

Doctor Charles Edwards, Commissioner of Food and Drugs, Department of HEW, and Doctor Malcolm Moos, President of the University of Minnesota, will be guest luncheon speakers at this year's meeting. The annual banquet has been scheduled for Thursday, May 18, at the Kahler Hotel. Members who have completed fifty years in the practice of medicine in the State of Minnesota will be accepted into the membership of the Fifty Club of the Minnesota State Medical Association. Many of the more than fifty scientific and non-scientific committees of the Association have scheduled breakfast meetings in conjunction with the Anuual Meeting, and physicians are urged to attend and take an active role in the affairs of their respective committees.

Business Sessions Set

The Thursday-Friday scientific program marks a departure from the traditional beginning of the week dates in previous years. Prior to this beginning of the scientific program, the House of Delegates will convene for its opening session Wednesday, May 17, at 1:00 P.M. in the Kahler Hotel. Reference Committees will meet following the opening session of the House to consider resolutions, officers and councilors reports, reports of committee chairmen, etc. The second session of the House will convene Friday, May 19 at 2:00 P.M.

Minnesota Chapter of the Flying Physicians Association

Luncheon Meeting—Saturday, May 20, 12:00 Noon, Gold Room of the Holiday Inn Downtown, Tickets: $4.25. All physicians interested in flying are inivited to attend. Advance reservations requested. Contact: Alex Webb, Jr., M.D., 311 Terminal Building, Mpls.-St. Paul International Airport, or Frank J. Bonello, M.D., 1074 So. Robert Street, W. St. Paul.

Woman's Auxiliary

The Woman's Auxiliary will observe its 50th anniversary at its annual meeting held in conjunction with the annual meeting of the Association in Rochester. The tentative program is as follows: Thursday, May 18—Executive Board Meeting and Luncheon, Kahler Hotel. Afternoon Tea—Mayo Foundation House. Friday, May 19—Annual Meeting, Kahler Hotel—Luncheon, Rochester Golf Country Club. General arrangements are being made by Mrs. Philip E. Bernatz and Mrs. James A. Bastron, Rochester.

1972 Tentative Program Timetable

Wednesday, May 17

1:00 P.M.	House of Delegates First Session—Kahler Hotel
4:30 P.M.	Reference Committees—Kahler Hotel
6:00 P.M.	Delegates and Councilors Dinner—Kahler Hotel
8:00 P.M.	Reference Committees Reconvene—Kahler Hotel

Thursday, May 18

7:30 A.M.	Committee Breakfasts—Kahler Hotel
8:00 A.M.	Registration—Mayo Civic Auditorium
9:00 A.M.	Scientific Session Begins—Mayo Civic Auditorium
12:15 P.M.	Luncheon—Kahler Hotel
2:00 P.M.	Scientific Sessions Continue-Afternoon Panels—Mayo Civic Auditorium and Art Center
6:00 P.M.	President's Reception—Kahler Hotel
7:00 P.M.	Annual Banquet—Kahler Hotel

Friday, May 19

7:30 A.M.	Committee Breakfasts—Kahler Hotel
8:00 A.M.	Registration—Mayo Civic Auditorium
9:00 A.M.	Scientific Session—Mayo Civic Auditorium
12:15 P.M.	Luncheon—Kahler Hotel
2:00 P.M.	Scientific Sessions Continue-Afternoon Panels—Mayo Civic Auditorium and Art Center
2:00 P.M.	House of Delegates Second Session—Kahler Hotel

Saturday, May 20

Specialty Group Meetings—
Specialty groups will be holding their annual meetings in conjunction with the Association Annual Meeting, Friday and Saturday.

Scientific Program

1972 Annual Meeting Minnesota State Medical Association

Thursday

9:00- 9:15 A.M. Laparoscopy—Jack E. Wall, M.D.

9:00- 9:15 Vesicoureteral Reflux—Panayotis P. Kelalis, M.D.

Retrograde flow of urine to the kidneys is closely linked to urinary infection. The incidence of vesicoureteral reflux is high in the first five years of life and then decreases sharply. Therefore, reflux is not a permanent phenomenon in all instances, and in many cases it may simply represent delayed maturation of the ureterovesical angle.

9:00- 9:15 Exercise as Treatment in Coronary Heart Disease—James I. Thompson, M.D.

Exercise may result in a beneficial effect on the natural history of ischemic heart disease. The incidence of myocardial infarction recurrence and death, appears to be reduced. An exercise program is also helpful in improving exercise tolerance, and may be of psychological benefit. One-third of the patients are capable of training at exercise levels greater than walking and self care. An individual program can be prescribed to limit the level of exertion, below that used for exercise testing. Steady state exercises as walking or bicycling are best. The prescribed exercise is carried out for thirty minutes, at least three times a week. Progression of exercise level may be possible, after a stress test re-evaluation.

9:20- 9:35 Surgical Emergencies in the Newborn—Bernard J. Spencer, M.D.

9:20- 9:35 Emergency Medical Care From Accident Site to Hospital—Claude R. Hitchcock, M.D.

9:20- 9:35 Polychemotherapy of Lymphoma—Irving J. Lerner, M.D.

Current multidrug therapy differs from the previous approach in two major ways: (1) an effort is made to select drugs which have in common known antitumor effect against the malignancy to be treated, but differ in the forms of their toxicity, and (2) the drugs are administered in an intermittent or "pulsating" rather than continuous fashion.

9:40- 9:55 Fetal Monitoring—David L. Hill, M.D.

9:40- 9:55 Coronary Artery Surgery—Demetre M. Nicoloff, M.D.

Myocardial infarction with its immediate mortality and subsequent morbidity constitute a major medical problem for the young and middle-aged male in the United States. Prodromal symptoms that often precede infarction are angina of recent onset or an increase in the severity and frequency of occurrence of angina. With the coronary arteriography and aortocoronary saphenous vein bypass, a new approach has been made available to treat preinfarction angina or angina unresponsive to medical therapy. The procedure offers an immediate and possibly, a lasting, increase in myocardial blood flow.

9:40- 9:55 Use of L-Dopa in Parkinson's Disease—Lawrence A. Farber, M.D.

10:00-10:10 Hyperbilirubinemia of the Newborn—Charles W. Jarvis, M.D.

10:00-10:10 Hemorrhoids: Surgery vs No Surgery—William T. Smith, M.D.

These past twenty-five years the most recommended treatment for hemorrhoids is surgery. This involves a hemorrhoidectomy that removes all varicosities, both internal and external, down to the sphincter mechanism and the circular muscle of the rectum. If residual hemorrhoids remains, ordinarily they will hypertrophy and become symptomatic. If hemorrhoids are properly removed, recurrence is minimal. Whenever injection treatment or ligation is used, the external hemorrhoids still have to be dealt with. These may be excised one at a time in the office using a local anesthetic and may require several patient visits. The best treatment offered to the low risk surgical patient is a one stage surgical excision of all the internal and external hemorrhoids using one of several standard techniques which destroys all anal-dermal and submucosal varicosities. One suggestion that has been made is that perhaps the entire problem of hemorrhoids could be resolved if man returned to quadrupedism.

Thursday (continued)

10:00-10:10 *Can Gallstones be Dissolved Medically?—Johnson L. Thistle, M.D.*

Most gallstones are composed predominantly of cholesterol. This lipid is normally excreted in bile, an aqueous solution, and is solubilized by incorporation into aggregates of bile acid molecules called "micelles." The capacity of these micelles to dissolve cholesterol is limited but is greatly increased by inclusion of the phospholipid, lecithin. Preliminary obervations have demonstrated disappearance of gallstones in one patient and marked decrease in stone size in three others after 6 to 22 months of treatment.

10:45-11:00 *Occular Complications of Commonly Used Topical and Systemic Medications—Dennis M. Robertson, M.D.*

Physicians must be alert to possible complication of commonly used medications.

10:45-11:00 *Surgical Treatment of Thyroid Nodules—Oliver H. Beahrs, M.D.*

A thyroid gland, diffusely firm and nodular, suspected of being Hashimoto's Thyroiditis, may be biopsied by a Silverman needle. If the diagnosis is correct, treatment is thyroid replacement therapy. Fibrous (Riedel's) thyroiditis may be indistinguishable from cancer and must be explored. The incidence of cancer in nodular goiters surgically removed is about 12-15%.

10:45-11:00 *Ambulatory Emphysema—Frank M. MacDonald, M.D.*

11:05-11:20 *Management of Malignant Melanoma—John C. Ivins, M.D.*

Cutaneous melanoma is a major malignancy for which there is no satisfactory therapy. It has a deserved reputation for being the most biologically erratic cancer with which we have to contend. For this reason, retrospective studies reporting three, five, and even ten year "cures" do not mean much in terms of deciding what constitutes adequate treatment. There are many reported instances of spontaneous regression of proven melanoma. There are even more instances of widespread metastases involvement without a known primary source, and many records relate the first appearance of metastases fifteen or more years after excision of the primary lesion. One of the urgent problems to be solved is the relationship of the regional lymph nodes to the course of the disease. The value of lymphadenectomy can probably be resolved only by prospective study, subjecting comparable patients to different treatment programs.

11:05-11:20 *Diagnosis of Diffuse Pulmonary Disease with Emphasis on Transbronchial Lung Biopsy—Howard A. Andersen, M.D.*

11:05-11:20 *The Current Treatment of Gout—Roger S. Colton, M.D.*

Effective agents for pain relief and reduction of inflammatory response includes Colchicine, Butazolidin, and Indocin. These drugs may be used as well in an attempt to prevent recurrent acute attacks. Equally as important is immobilization and complete rest of the joint or joints involved. Hot and/or cold packs, whichever gives symptomatic relief, and narcotics as needed initially are helpful adjuncts. Reduction of total body urate is done by uricosuric agents such as Probenecid (Benemid), Sulfinpyrazone (Anturane), or high doses of salicylates; Xanthine oxidase inhibitors (Zyloprin) also lower serum uric acid by inhibiting the metabolic formation of uric acid.

11:25-11:40 *Management of Asthma—James P. Lillehei, M.D.*

11:25-11:40 *Surgical Treatment of Early Lung Cancer—Josiah Fuller, M.D.*

"Early Lung Cancer" does not describe a time period but refers to the stage of the disease and is an important factor in determining the extent of surgical therapy. The more differentiated squamous and adenocarcinomas respond better to surgical therapy than the undifferentiated bronchogenic carcinomas. Small cell bronchogenic carcinoma is rarely resectable. Surgical treatment should be the minimal resection commensurate with complete removal of all cancer. When the circumstances indicate, aggressive surgical therapy including mediastinal lymph node dissection and chest wall resection should be carried out. The five year survival rate for surgically resected bronchogenic carcinomas compares favorably with that of many other internal cancers. The number of major thoracotomies for inoperable bronchogenic carcinomas should be kept to a minimum. Anterior mediastinotomy is a simple and useful procedure for determining operability of lung cancer.

Thursday (continued)

11:25-11:40 *Recurring Urinary Tract Infection in Women—Lynwood H. Smith, Jr., M.D.*

11:45-11:55 *Upper Airway Problems in Anesthesia—Joseph J. Buckley, M.D.*

11:45-11:55 *The Aggressive Approach to Asymptomatic Cholelithiasis—Edward S. Judd, M.D.*

The extreme medical view holds that surgery for "silent" gallstones cannot be defended. The extreme surgical view urges cholecystectomy for every case of gallstones. We advise careful consideration of the operative risk of early elective surgery, versus the risk of later elective surgery and even emergency surgery for increasing symptoms. Autopsy studies reveal that 23 percent of males and 46 percent of females between the ages of 70 and 79 years have gallstones. Retrospective survey proves symptoms existed in 40 percent of the patients. A study here concerning 112 patients who were found to have incidental gallstones, reveals 25 percent developed dyspepsia and 20 percent developed colic. Forty-five percent developed significant symptoms of some kind. In another study of 34 "silent gallstone" cases, one out of five developed serious complications later. For younger patients we advocate prophylactic cholecystectomy. For the aged patient, we must individualize considering the life expectancy, the greater operative risk, and the competing risks.

11:45-11:55 *The Irritable Colon Syndrome—William D. Blackwood, M.D.*

The vulnerability of the gastrointestinal tract to adverse life situations is reflected in the frequency with which the irritable colon syndrome is seen. The common symptoms of bloating, pressure, pain, flatulence and alternating diarrhea and constipation with relief by emptying the colon appear to be related to abnormal motility and exaggerated normal physiologic activity. Motility studies have clarified some of the mechanisms of symptom production.

Friday

9:00- 9:15 A.M. *New Antibiotics—Robert P. Gruninger, M.D.*

9:00- 9:15 *Current Treatment of Gonorrhea—Arnold L. Schroeter, M.D.*

Controlling the gonorrhea epidemic in the United States will depend on adequate antibiotic treatment of the infected patient. Despite partial antibiotic gonococcal resistance, procaine penicillin G is still the treatment of choice. Although many partially antibiotic-resistant gonococcal strains have been imported from the Orient, most of our resistant strains have been developed in the United States by inadequate treatment schedules.

9:00- 9:15 *Neurosurgery: New Methods for Pain Control—Donlin M. Long, M.D.*

9:20- 9:35 *Chemotherapy of TB—David T. Carr, M.D.*

The chemotherapy of tuberculosis is truly one of the miracles of modern medicine. Presently available drugs are so effective that cure of the disease is not only to be expected but should be demanded. The death rate attributed to this disease should fall to zero if every case were diagnosed before the patient was moribund, the proper regimens of drug prescribed, and the drugs taken faithfully by the patient.

9:20- 9:35 *Evaluation of Borderline Hypo- and Hyperthyroidism—Alvin L. Schultz, M.D.*

I^{131} uptake has been suppressed by the addition of iodide to commercial breads. The mean value at 24 hours in euthyroid persons has been reduced to 13 to 15% and the upper limit of normal is probably no more than 30%. Values above 25% should be considered suspicious of hyperthyroidism. Thyroid I^{131} uptake has become of little value in the diagnosis of hypothyroidism because of the lowered normal values. Serum protein-bound iodine is being replaced by the measurement of serum thyroxine by saturation analysis (Murphy-Pattee), a much more sensitive and reliable method for the diagnosis of both mild hypo- and hyperthyroidism. Measurement of serum free thyroxine and free triiodothyronine are now possible and may be the most sensitive means for the diagnosis of mild hyperthyroidism. Mild hypothyroidism has always been difficult to diagnose on clinical or laboratory grounds. The

Friday (continued)

availability of a reliable measurement of serum thyrotropin (TSH) by radioimmunoassay is proving to be the most sensitive and effective way to diagnose early and mild primary hypothyroidism. TSH levels become elevated very early in the course of primary hypothyroidism usually before clear-cut clinical signs are apparent. The recognition that hyperthyroidism can be produced by elevation of triiodothyronine without an associated increase in serum thyroxine explains some of the cases which in the past have been confusing to the clinician.

9:20- 9:35 *Plastic Surgery: Snowmobile Injuries—Conrad I. Karleen, M.D.*

9:40- 9:55 *Urinary Tract Infection in Children—Warren J. Brooker, M.D.*

Urinary tract infection frequently causes childhood illness. It is among the most common sources of fever in children. Complete urologic evaluation including cystogram, IVP, and endoscopy is indicated in all boys with infection. Girls with repeated or persistent pyuria, all cases in which the cultured organism—proteus or pseudomonas—suggests chronicity, and all children with hematuria or "sterile" pyuria also require investigation. *Relative* indications are "failure to thrive", anema, azotemia, hypertension, auricular, or genital anomalies, and suggestive family history. Pyelonephritis is an incomplete diagnosis inasmuch as there is "always" an associated anatomic or physiologic defect which must be corrected to effect a cure. Treatment must include a systemically effective drug during the septic state, surgical correction of anatomic defects and suppressive drug therapy for a prolonged period during recovery.

9:40- 9:55 *Ear, Nose, Throat: Trauma to the Larynx—Jerome A. Hilger, M.D.*

9:40- 9:55 *Recent Advances in Cancer Treatment—Radiation Therapy—Seymour H. Levitt, M.D.*

10:00-10:10 *Alternate Day Corticosteroid Treatment—Richard G. VanDellen, M.D.*

Despite complications of steroid drugs, they remain effective and necessary therapy for some patients with asthma, pemphigus, nephritis, rheumatoid arthritis, and other diseases. Prednisone administered by a single morning dose on alternate days does not suppress the adrenal-pituitary axis. A single dose of steroids given on alternate days causes fewer side-effects than comparable doses given daily. Prednisone, prednisolone, or methylprednisolone should be used on alternate days but not triamcinoline or dexamethasone, both of which have a longer suppressive effect on the pituitary-adrenal axis. Hydrocortisone and cortisone have not been used because of sodium retention. Alternate-day steroid therapy is effective in patients with asthma. After first controlling the asthma with daily doses of steroids, alternate-day therapy is instituted. Forty mg of Prednisone by mouth in one dose to be taken in the morning every other day. Decreased 5 to 10 mg every fourth to sixth dose is typical although 80 to 120 mg every other day have been used with minimal side effects. Preliminary evidence suggests that diseases such as lupus erythematosus, nephritis, and pemphigus also may be controlled by steroids taken every other day.

10:00-10:10 *Urographic Techniques in the Diagnosis of Renal Masses—Elwin E. Fraley, M.D.*

10:00-10:10 *General Surgery: Hyperalimentation, Intravenous—Robert L. Telander, M.D.*

10:45-11:00 *The Diagnosis and Treatment of Nocturnal Enuresis—Daniel C. Merrill, M.D.*

The bladder function of 39 enuretic children was evaluated with air cystometry. Approximately 50 percent of these children had normal bladder function for age. The remaining had reduced bladder capacities. Bedwetters with normal bladder function usually were deep sleepers while enuretics with small bladder capacities had normal sleep patterns. Deep sleepers with normal bladder function were treated with conditioned response therapy. Children with small bladder capacities were treated with holding exercises and Tincture of Belladonna. Eighty percent of the entire group were cured (21 consecutive dry nights). Twenty percent relapsed, this group usually responded to a second short period of conditioned response therapy.

Friday (continued)

10:45-11:00 *Serum Multiple Analysis Patterns in Diagnosis of Disease—Richard L. Reece, M.D.*

New technology, (multichannel chemical analyzers, multitest hematology instruments, and computers) makes pattern recognition of disease inevitable. You can now do many tests inexpensively, rapidly, and accurately on one sample. Given many results together, you begin to perceive patterns: clusters of abnormals that occur in disease states, in non-fasting specimens, or after certain drugs. You see results in perspective rather than in isolation. You see patterns.

10:45-11:00 *Gynecology: Vaginal Hysterectomy in Younger Women for Sterilization—Tiffany J. Williams, M.D.*

11:05-11:20 *"Brittle" Juvenile Diabetics Often Are Victims of Unrecognized Compensatory Hyperglycemia—the Somogyi Effect—Henry S. Sauls, M.D.*

About 3% of insulin dependent diabetics are difficult to regulate. Management problems have been induced by over-treatment with insulin in about 15% of juvenile diabetics attending classes at the Diabetes Education Center.

11:05-11:20 *Treatment of Hyperlipidemia—John L. Jnergens, M.D.*

11:05-11:20 *General Surgery: Bile Acid Metabolism: Surgical Significance—Alan F. Hofmann, M.D.*

The surgical significance of bile acids is as follows: (1) virtually all patients with resection or bypass of the terminal ileum have bile acid malabsorption and a compensatory increase in synthesis; the increased passage of bile acids into the colon causes a watery diarrhea which responds to cholestyramine. (2) In patients with large resections of the ileum, interruption of the enterohepatic secretion of bile acids causes fat maldigestion and fat malabsorption. Removal of fat from the diet (made possible by equicaloric replacement with medium chain triglyceride) may improve diarrhea. (3) A new syndrome of hyperoxaluria associated with nephrolithiasis has been noted in patients with ileal resection. This appears to be related to increased conjugation of bile acids with glycine and may respond to oral taurine therapy. (4) Cholesterol cholelithiasis is associated with a diminished bile acid pool. (5) In patients with stagnant intestinal loops, bacterial overgrowth causes increased bile acid deconjugation leading to decreased concentration of conjugated bile acids.

11:25-11:40 *Current Concepts in the Treatment of Osteoporosis—David L. Hoffman, M.D.*

Involutional (postmenopausal or senile) osteoporosis is still of unknown cause, although it appears that age, sex, race, calcium intake and absorption, gonadal function, and skeletal stress all play a role in its development. Treatment has been largely empirical with a strong placebo effect suspected with almost all modes of therapy.

11:25-11:40 *Choice of Treatment in Patients with Hypertension—Louis A. Tobian, M.D.*

11:25-11:55 *Orthopedics: Total Hip and Other Joint Replacement—Mark B. Coventry, M.D.*

11:45-11:55 *Cutaneous Clues to Systemic Malignancy—Harold O. Perry, M.D.*

One must identify the skin reaction as specifically as possible. This might require the use of skin biopsy or immunofluorescent techniques. Some patients with cutaneous alterations based on hereditary patterns who have developed malignant disease have altered immunologic competence on appropriate laboratory testing. Cases illustrating cutaneous lesions indicative of systemic malignant disease wll be presented.

11:45-11:55 *Clinical Assessment of "Bleeders"—William R. Swaim, M.D.*

Bleeding is due to defects in blood vessels, platelets or plasma coagulation. The nature of the bleeding is helpful in diagnosis. Platelet and/or vascular abnormalities are associated with superficial bleeding such as petechiae, epistaxis, menorrhagia, and gingival bleeding. Patients with plasma coagulation abnormalites more commonly have deep bleeding such as hemarthroses and muscle hematomas. If disseminated intravascular coagulation is considered then additional tests that may be helpful include a thrombin time, fibrinogen and fibrin split product assessment, detection of fibrinonomer by the serially diluted protamine sulfate test, fibrinogen quantitation and if available a factor V assay.

Thursday Afternoon — Panels

2:00- 5:00 P.M. *The Recognition and Management of the Dependent Person—Subcommittee on Alcoholism and Drug Abuse of the Committee on Mental Health, Minnesota State Medical Association—Myron R. Wilson, Jr., M.D. Program Chairman*

The Subcommittee of Drug Abuse and Alcoholism will focus on the person, not the problem, in the scientific presentation at the Annual Meeing this May. The forum will include a general discussion of dependency in persons, and specific clinical situations will describe the means by which physicians can detect manifestations, recognize symptoms, and treat the person, who is suffering from dependent related problems.

2:00- 3:00 *Surgical Treatment of Dumping Syndrome—Martin A. Adson, M.D., Chairman; Panel Members—Henry Sosin, M.D., Michael M. Eisenberg, M.D., William D. Blackwood, M.D.*

2:00- 3:00 *Arrhythmias, Blocks, Pacemakers—Yang Wang, M.D., Chairman; Panel Members—Edward A. Ryan, M.D., A. McDonnell Richards, M.D., John P. Stokes, M.D.*

A brief ten-minute talk by each of the panel members as planned and then a panel discussion during which questions will be welcomed from the audience will be held.

2:00- 3:00 *Meet the Medical School Deans—H. Drew Miller, M.D., Chairman; Panel Members—Robert E. Carter, M.D., Ward S. Fowler, M.D., Mead Cavert, M.D.*

2:00- 3:00 *Transient Cerebro-Ischemic Attacks—Clark H. Millikan, M.D., Chairman; Panel Members—Arthur C. Klassen, M.D., Robert G. Siekert, M.D., Thoralf M. Sundt, Jr., M.D., Jack P. Whisnant, M.D.*

Transient cerebral-ischemic attacks are the most significant events warning that a stroke can happen. This panel will describe the importance of the attacks and how the diagnosis is established.

3:45- 5:00 *Surgical Management of Biliary Tract Problems—Donald C. McIlrath, M.D., Chairman; Panel Members—John P. Delaney, M.D., James J. Monge, M.D., Frederick M. Owens, Jr., M.D.*

Common problems encountered in surgery of the biliary tract will be considered with particular emphasis on the practical aspects of evaluation and treatment. Case histories illustrating the preoperative and operative problems will form the basis for discussion.

3:45- 5:00 *Hepatitis Associated (Australia) Antigen—Jeffrey McCullough, M.D., Chairman; Panel Members—John M. Matsen, M.D., Herbert F. Polesky, M.D., Howard F. Taswell, M.D., Johnson L. Thistle, M.D.*

3:45- 5:00 *Psychiatric Aspects of Pain—Maurice J. Martin, M.D., Chairman; Panel Members—Loran F. Pilling, M.D., Neil Yorkston, M.D., Lawrence R. Gowan, Jr., M.D.*

The problem of pain will be discussed by a panel of psychiatrists from various portions of Minnesota who are exposed to various types of practice. Various aspects of the problem including evaluation, diagnosis and therapy will be discussed. It will be emphasized that emotional aspects of pain contribute signifcantly to the perception of pain and consequently to its appropriate management. If the physician understands the emotional components and the meaning of pain to the patient, he will be in a better position to treat the patient and his symptom.

3:45- 5:00 *Mesenteric Vascular Disease—Mesenteric Arteriography—Owings W. Kincaid, M.D., Chairman; Panel Members—Kurt Amplatz, M.D., Thomas E. Johnson, M.D., Douglas B. McGill, M.D., Philip E. Bernatz, M.D.*

Vascular lesions of the mesenteric vessels, some of which may result in bowel ischemia or infarction, will be considered from the standpoint of symptomatology, radiographic and arteriographic diagnosis, and surgical treatment.

Friday Afternoon—Panels

2:00 -5:00 *Environmental Health—MSMA Committee on Environmental Health. Guest Speakers—Robert D. Moseley, Jr., M.D., William R. Fifer, M.D., Hymie Gordon, M.D., Mr. George S. Michaelson.*

The Committee on Environmental Health will focus its discussion on five environmental health topics: With its guest speakers, they will cover: (1) environmental health problems in medical practice and the hospital, (2) solid wastes and disposal, (3) radioactive sources, (4) contamination and infection and (5) the physician and population control.

2:00- 3:00 *Oral Hypoglycemic Agents—Frederick C. Goetz, M.D., Chairman: Panel Members, E. B. Cohen, M.D., Clifford Gastineau, M.D.*

The panelists will present an outline of their current practice in the use of oral hypoglycemic agents in the adult type of diabetes.

2:00- 3:00 *Massively Injured Patient—John F. Perry, Jr., M.D., Chairman; Panel Members—James H. House, M.D., Donald L. Erickson, M.D., Claude R. Hitchcock, M.D., Alexander S. Cass, M.D.*

The format of the panel discussion will be to present case histories and x-rays of patients with massive injuries. These will be chosen to illustrate surgical, orthopedic, neurosurgical and urological problems encountered in this situation. Emphasis will be primarily upon diagnostic procedures and initial treatment to be employed in the massively injured patient. Priorities for treatment of individual injuries in the multiple injury situation will be discussed also.

2:00- 3:00 *Epilepsy in Children—Robert V. Groover, M.D., Chairman; Panel Members—Kenneth F. Swaiman, M.D., Jerrold Milstein, M.D.*

This hour will be devoted to a discussion of the clinical classification, differentiation, and management of seizures in infants and children by the panel members. Particular emphasis will be placed upon neonatal seizures, "febrile seizures", clinical features of various seizure types, and the differential points between generalized and focal seizures.

2:00- 3:00 *Carcinoma of the Ovary—Konald A. Prem, M.D., Chairman; Panel Members—Leon L. Adcock, M.D., George Malkasian, Jr., M.D., Thomas K. Jones, M.D.*

Dr. Adcock will speak on Surgical Management, Dr. Malkasian on Chemotherapy and Dr. Jones on Radiotherapy of Carcinoma of the Ovary. Each presentation will be approximately 10-15 minutes. A few minutes at the end will be devoted to questions from the audience.

3:45- 5:00 *Diagnosis and Management of the Patient with an Ischemic Extremity—James R. Pluth, M.D., Chairman; Panel Members—Edward A. Ryan, M.D., Joseph C. Kiser, M.D., Jui-Sung Hung, M.D.*

Surgical aspects of acute arterial injury and thrombosis will be presented in addition to the choice of procedures for providing revascularization of the chronic ischemic limb.

3:45- 5:00 *The Family Physician—Our Most Important Link in Early Identification of Vision and Hearing Problems—Panel Members—Robert J. Fink, M.D., James B. McBean, M.D., Robert T. Kelly, M.D., Mr. Allan Tingley, Mrs. J. E. Anderson.*

The importance of early detection of vision and hearing handicaps will be discussed, including the necessity of thorough examination by the family physician of patients to uncover such deficiencies.

Friday Afternoon—Panels (continued)

3:45- 5:00 *New Concept in the Care and Management of the Cerebral Palsied—Sponsored by United Cerebral Palsy of Minnesota—Speakers—Leon Sternfield, M.D., V. Richard Zarling, M.D.*

The research and training aspects of the Foundation with particular reference to how these might apply in Minnesota. The developments that are occurring, mobilizing the most severely and multiply handicapped in some of our institutions with particular reference to the work at Faribault State School in Minnesota. The presentations would be conducted on an "interview" type basis. This would involve essentially, three or four persons to be interviewed.

3:45- 5:00 *Medical Audit—James M. Schless, M.D., Chairman; Panel Members—William R. Fifer, M.D., Robert E. Hansen, M.D., Lorenzo D. Trajano, M.D., Laurence A. Savett, M.D., Richard E. YaDeau, M.D.*

The delivery of good medical care is a goal of all physicians. Maintaining quality in the face of rapid changes in biomedical knowledge and changing patterns and expectations of health care delivery must concern all practicing physicians. Objective methods of determining quality of care actually being delivered at the local level (hospital or office) are available to physicians through the educational audit and are greatly enhanced through use of the problem-oriented record. Objective evaluation in terms of changed patterns of patient care can be obtained by periodic recheck. A pilot program has been conducted in Minnesota in five community hospitals during the past year.

Gowers' Syndrome

This syndrome consists mainly of sensory and subjective attacks to which Gowers unfortunately and erroneously applied the adjective "vagal." The attacks occurred primarily in women, whose family history was tinged with migraine, epilepsy, or insanity.

Attacks were characterized by paresthesias, dyspnea, sometimes intense, precordial discomfort in the form of pain or palpitation, and a feeling of apprehension and dread. At times the pulse was small and almost imperceptible. Facial pallor, cramplike spasm, and even rigors were present. Gowers considered the etiology to be "a disturbance of the vasomotor center." The only significance of this syndrome is that it contributed to the differentiation and clarification of the clinical concept of the vasovagal syndrome. Gowers' syndrome has no counterpart in today's diagnostic terminology.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York



Book Reviews

ORGANIZATION AND ADMINISTRATION OF HEALTH CARE. Richard L. Durbin and W. Herbert Springall. The C. V. Mosby Company, St. Louis, 1969, 248 pages.

This book presents a comprehensive overview of all facets of hospital organization, management and administration. Part I develops the theoretical foundations of administrative science, including among others a discussion of the Hawthorne experiments. Part II deals with both the optimal organizational scheme of a hospital and the practical problems of reorganization. In Part III economic problems of resource allocation are analyzed. Part IV deals with various questions of implementation. Of special interest are the industrial engineering techniques discussed briefly such as workload and work flow studies, and a proposed classification system. Even the subtle subject of quality control is presented in a very readable way. Part V finally develops ideas for organizational development beyond traditional ways that merit close attention.

The exposition is lucid and stimulating throughout. Diagrams and examples and case material are used felicitously. The section on business and finance contains detailed illustrative worksheets and budgets. This book should prove a valuable aid to hospital administrators. But it can be recommended also to doctors as a fascinating and reliable guide to improved understanding of the complexities that beset modern hospital management. However, no panacea for solving the perennial problem of rising costs should be expected.

Martin Beckmann, Ph.D.
Brown University

ARTHRITIS AND PHYSICAL MEDICINE. Author: Sydney Licht, M.D. Publisher: Elizabeth Licht, East New Haven, Connecticut.

This monograph encompasses manuscripts by 21 authors, all of whom have the problems of arthritis. It is reasonably comprehensive for a disease in which the etiology and specific treatment continue to remain somewhat of a mystery.

It should serve as a good source of reference for its contents and in its bibliography. I find it well illustrated with suitable line drawings, photographs and X-rays.

Carl O. Rice, M.D.
Minneapolis, Minnesota

ADVANCED GASTROINTESTINAL CANCER—CLINICAL MANAGEMENT AND CHEMOTHERAPY. By Charles G. Moertel and Richard J. Reitemeier. Harper & Row, New York.

This book is divided into two parts with 208 pages of text and 8 pages of a useful and functional index.

The first section is devoted to Clinical Management of Advanced Gastrointestinal Cancer and presents a review of various symptoms produced by the disease; problems of edema and ascites, nausea and vomiting, and the relief of pain are covered by the primary authors. Additional sections are contributed by Dr. Martin A. Adson, who reviews the role of the surgeon in palliative management, and by Donald S. Childs, Jr., on the radiation therapist and his role in palliative management. Dr. Uihlein writes on the function of the neurosurgeon, and Dr. Allen B. Gould on the role of the anesthesiologist. The philosophy of terminal care, the symptomatic relief of the numerous problems such as anemia, biliary obstruction, partial bowel obstruction, nutritional deprivation are included and some useful suggestions made. Finally, surgical and other palliative therapy is evaluated on the basis of changes or improvements in the natural history of the disease itself.

The second part of the text is devoted to Chemo-Therapy of Advanced Gastrointestinal Cancer and it begins with an evaluation of the greatest problem to the practicing physician, namely, the selection of patients for chemotherapy. The criteria for evaluation of results are presented in a forthright, scientific manner, followed by the specifics directed at each of the various types of drugs in current use. It is noteworthy that 45 pages are devoted to five fecal urobilinogen and 50 pages to all the other chemical substances combined. One helpful section reviews regional perfusion and another, chemotherapy combined with x-ray.

This volume makes a very worthwhile text for treatment and decision regarding referral of patients with advanced gastrointestinal cancer.

J. H. Strickler, M.D.
Minneapolis, Minnesota

ESSENTIALS OF CLINICAL ENDOCRINOLOGY by Norman G. Schneeberg; The C. V. Mosby Company, St. Louis, 1970, $22.50, 440 pages.

A well qualified author and eight contributing authors have efficiently dealt with all of the major endocrine problems as adequately as it is possible to do. The complexities of the numerous chemochemicals that are involved in endocrinology and the biogenesis of many of these have been compounded by the extensive use of the abbreviation system. Fortunately an appendix of these has been included; but for the usual reader a complete spelling of each of these abbreviations would, in all probability, provide a smoother flow of thought than is possible for one who must keep clearly in mind the meaning of a dozen or so acronyms for each chapter, and a new set for the next chapter.

The book is beautifully bound, adequately illustrated, nicely indexed and a credit to the author. For the endocrinologist it is an up-to-date masterpiece. For the practicing physician it is an excellent reference.

Carl O. Rice, M.D.
Minneapolis, Minnesota

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Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

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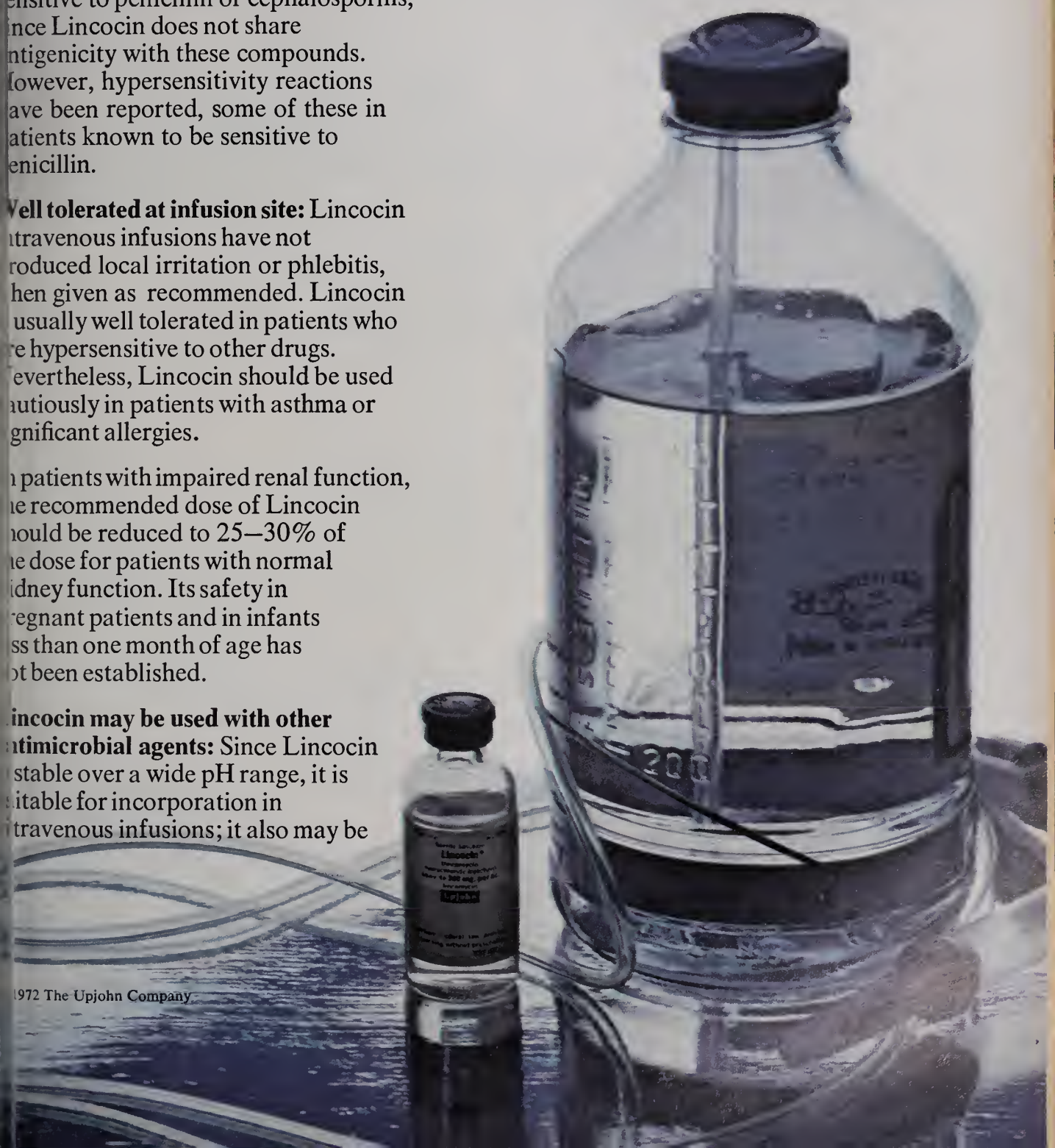
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Fracture Conference

Nonunions of the Humeral Shaft*

Darrell E. Fisher, M.D.:

Previously, fractures of the humeral shaft were discussed in relation to multiple injury, infection, and radial-nerve involvement. The present discussion will consider such fractures only in relation to the problems of nonunion itself. Prior to 1940, humeral-shaft fractures accounted for the greatest number of nonunions in long bones. In 1940 Caldwell reported the use of the hanging cast in this fracture, which he had used since 1933. This technique revolutionized previous cast techniques; nonunion of the humerus no longer was as difficult a problem. Stewart and Hundley[1] from the Campbell Clinic reported on 223 humeral-shaft fractures, including all types of fractures and associated injuries, and found only five with nonunion. In these cases, nonunion was considered to be due to distraction by hanging casts that were too heavy. They recommended appropriate hanging casts for all humeral fractures regardless of their level.

Nonunion of any long bone can be a problem, not only in definition and diagnosis but also in treatment. Nonunion is essentially a halt in the normal process of repair in fracture healing. It is often considered in relation to time alone; whereas, in fact, it is a pathologic change. Frequently, a delayed union is considered a nonunion, when actually the processes of healing are proceeding by x-ray and clinical assessment, even though more slowly than usual. Nonunion may become apparent at any time (Table 1). Clinical

*Fracture Conference, May 19, 1969.

TABLE 1

Symptoms and Signs of Nonunion in Femoral-Shaft Fractures

Clinical	X-ray	Histologic
Pain	Defect in continuity	Interposed fibrosis
Edema	Sclerosis of bone ends	No trabecular bridge
Local temperature	"Rounding"	Necrotic bone ends
Motion or crepitus	"Mushrooming"	Pseudarthrosis
Conduction of vibration	"Tapering"	
	Medullary occlusion	
	Stress test motion	
	Serial films	

TABLE 2

Factors Related to Fracture Union and Nonunion

Treatment Factors	Inherent Factors
Reduction	Site (cortical or cancellous)
Immobilization	Type (oblique, spiral, transverse)
Distraction	Comminution or bone loss (or both)
Compression	Compounding
Surgical intervention	Infection
	Interposition of soft tissue
	Blood supply
	Local pathologic changes
	Age of patient
	General condition

examination often indicates nonunion, but roentgenography is the usual means of diagnosis. Of course, histologic material will confirm the diagnosis. All degrees of union are seen; and in delayed union the patient is frequently treated before frank nonunion develops. Numerous factors determine whether or not fractures unite (Table 2). There is obvious connection between the treatment factors and the inherent factors.

The time of clinical and x-ray union in the humerus was illustrated in a series of 87 patients. In 10 weeks, 75% of the patients had clinical union and most had x-ray union. Several groups have studied the causative factors of nonunion in fractures of the shaft. In a series of 2,700 shaft fractures of all kinds at the Research Hospital in Illinois,[2] the most common factors in 127 nonunions were inadequate initial reduction, interposition of soft tissue, distraction, and improper surgery. Mnaymneh, Smith-Petersen, and Aufranc[3] analyzed 47 humeral-shaft nonunions at Massachusetts General Hospital. The order of frequency of fractures affected was: (1) those in the middle third of the shaft, (2) those that were either compounded or comminuted (or both), and (3) those that had had primary open reduction. They believed that all three of these fracture types were related to blood supply.

In this respect, Laing[4] did a definitive study on the blood supply to the adult humerus, using injections of barium sulfate in adult cadavers (ages 30 to 80 years). In this group of 30 cadavers he found that a single artery supplied the nutrient vessel in 28 and that two or more smaller arteries supplied the bone nutrient vessels in the other two. The nutrient artery was a direct branch of the brachial artery in more than 20 cases and entered the medial and anterior portion of the shaft at the junction of the middle and lower thirds in nearly all cases. This work emphasizes the dangers of ischemia after fracture in the middle and distal thirds not only during the fracture itself but also during any surgery performed in this region. Laing concluded that blood supply is the single most critical factor in relation to nonunion of the humerus.

In 1935, Ghormley and Mroz[5] reported the results in 341 cases of humeral-shaft fracture seen at the Mayo Clinic from 1926 to 1930, prior to the time of the use of the hanging cast. Fractures at all levels were represented. They believed that the most common causes of nonunion were inadequate fixation and too brief periods of immobilization. They found that the humeral shaft was the most difficult of all long bones to hold and to fix initially. Watson-Jones[6] believes that inadequate type or length of immobilization is the cause of all nonunions. I am not so sure we would agree with him.

Case 1

Dr. Fisher:

A 50-year-old nurse, on March 25, 1968, fell down three steps and suffered a slightly comminuted spiral fracture of the right humerus. There was no other attendant injury. She was treated with a hanging cast for 10 weeks and nonunion was diagnosed from clinical and x-ray evidence.

In July 1968, she came to the Mayo Clinic, at which time she had pain and crepitation, and x-ray evidence of nonunion (Figure 1*A*). On July 16, 1968, through an S-curved incision, the pseudarthrosis was excised, medullary canals were reamed, and an onlay tibial graft, 1½ by 9 cm, was held with six screws. The fracture itself was fixed with two screws (Figure 1*B*). Cancellous chips of bone were added and a well-fitted Velpeau dressing was used. The dressing was changed weekly for the next couple of months, during which time she had severe, acute thrombophlebitis. By October—three months after internal fixation—the roentgenogram showed evidence that the grafts were incorporating. Her elbow and her shoulder

were developing motion. The last film taken four months after internal fixation showed sound healing (Figure 1*C*). Her elbow could move from 50° to 150°, and she had only minimal stiffness of her shoulder.

John C. Ivins, M.D.:

Could we see the initial before-treatment x-ray? Did you describe the general appearance of this patient as essentially round, not too fat, but a lot too short? You can see from this x-ray (Figure 1*A*) that everything about her is big and fat. I would like to know how some of my colleagues would initially treat a fracture like this in a patient with a similar body configuration. The reason I am asking the question is that, in such a fracture, I have never been able to use a hanging cast when the patient had a body build like this.

Mark B. Coventry, M.D.:

I would think you could. Why not?

Dr. Ivins:

The hanging cast does not hang properly because of the patient's body build.

James H. Dobyns, M.D.:

You can move the breast out of the way, or you can build a little shelf.

Dr. Coventry:

But you have some abduction because of the breast and you have gravity working for you.

Dr. Fisher:

In this type of situation, Caldwell recommended the use of the abduction splint or sometimes a well-applied spica cast because of the body configuration.

Einer W. Johnson, Jr., M.D.:

Is it more a problem of body configuration or of the proportion of fat versus muscle in this hanging arm? If the weight of the forearm is greater than the power of the muscles in the upper arm, then the hanging cast will fail because these muscles are overpulled and distraction of the fragments will occur. The breast does not put as much distracting force on the fracture as the weight of the forearm does.

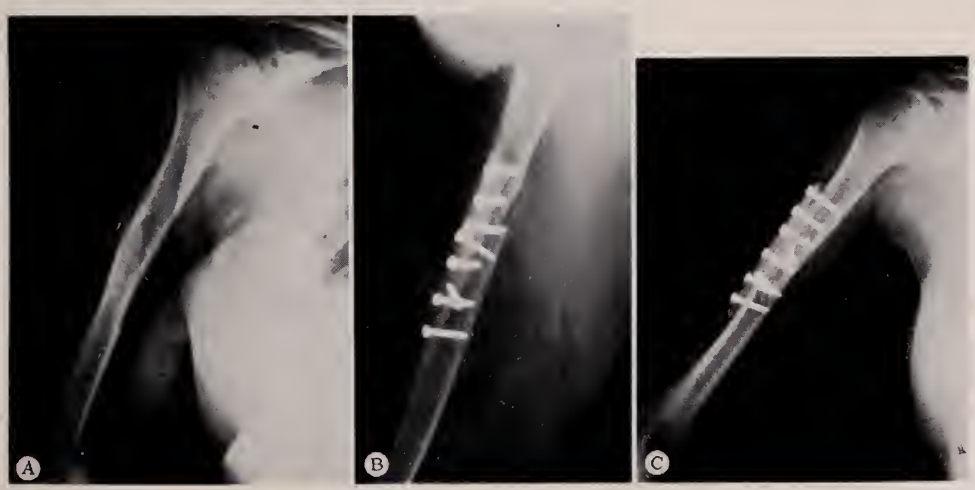


Fig. 1—(Case 1). *A*, Nonunion of comminuted spiral shaft fracture 14 weeks after initial treatment in hanging cast. *B*, Postoperative internal fixation with tibial onlay graft and eight screws. *C*, Clinical and x-ray union four months after internal fixation.

Dr. Ivins:

As far as I am concerned, the problem is a mechanical one. It does not concern the breast only. When this patient, like all people with this type of body configuration, walks down the street, she holds her arms out at her sides like wings, because her arms simply will not come down. It has been my experience that, when these patients are treated by a hanging cast, they have intertrigo-like skin problems that are worse than the initial fracture.

Richard S. Bryan, M.D.:

I have treated one or two such patients with only a plaster splint and a Velpeau because, as Dr. Johnson has said, the arm is just too heavy.

Case 2

Dr. Fisher:

A 38-year-old lady, in an altercation with her husband on November 29, 1967, suffered a fracture of the distal third of the humerus. It was electively fixed internally on the day of injury with two small, threaded wires and some external support. Three months later without evidence of healing, the fracture was treated with two stainless steel screws in a similar manner; a cast and sling were used thereafter for six months. The following July—eight months after her injury— when seen at another clinic, she had extensive osteoporosis, Sudeck's atrophy involving her hand and arm (with considerable pain), and many skin changes. She came to the Mayo Clinic for another opinion 10 months after injury. At that time she had severe pain, 10° of motion in the elbow, 20° in the shoulder, and a history of an allergy to nearly all metals, including gold and silver (Figure 2*A* and *B*). She was very difficult to handle throughout the entire course of treatment, as was her husband, who added to an already serious problem.

Dr. Ivins:

Will someone comment about the initial treatment of a fracture like this? This is a closed fracture with no soft-tissue injury and a very short distal humeral fragment. What is the proper initial treatment for this fracture? Is this a fracture that can be treated by a hanging cast?

Dr. Dobyns:

I seldom use a hanging cast. I might use a Velpeau dressing or a splint. I would want to make sure that I approximated the fragments and did not distract them.

Dr. Ivins:

On the assumption that there were no soft-tissue injuries or other extenuating circumstances, would you use open reduction?

Edward D. Henderson, M.D.:

I think that you can open it if you have some justification, but if you did an open reduction, you would have to apply adequate internal fixation—with a plate for example.

Dr. Ivins:

This case, like many, was not simply one of a fracture. There were extenuating circumstances. Therefore one must be reserved in criticizing the previous treatment. This fracture was produced by physical combat between man and wife, and after the doctor had started the treatment at another institution, there was additional physical combat.

Dr. Coventry:

Still, two Kirschner wires are not adequate internal fixation under any circumstances, extenuating or otherwise.

Dr. Fisher:

On August 19, 1968, nine months after injury, the two screws were removed via the old posterior incision. No reaction was found around these screws. The pseudarthrosis was excised, the ends were squared to bleeding bone, and a four-hole compression plate with strip grafts of iliac bone was applied (Figure 2*C*).

Dr. Ivins:

In looking at this x-ray, keep in mind that the shoulder was completely stiff and that the elbow was virtually stiff.

Dr. Fisher:

Three months after the compression plate was applied, after extensive ef-



Fig. 2—(Case 2). *A* (anteroposterior), and *B* (lateral), Nonunion 10 months after injury and two unsuccessful attempts at internal fixation. *C*, Postoperative internal fixation with four-hole compression plate and autogenous onlay iliac bone grafts. *D* (anteroposterior), and *E* (lateral), Clinical and x-ray union eight months after bone grafting and compression fixation.

forts at physical therapy, and after psychiatric therapy for both husband and wife, the elbow had motion from 50 to 90°, but the shoulder was still almost completely stiff. The patient had considerable pain in the upper extremity, and this was a distressing problem. Four and a half months later, with therapy, her hand had progressed to near normal, as had her wrist. The elbow now had 65° of motion, and shoulder motion was at least noticeable. Films on April 23, 1969, eight months after internal fixation, showed much better range of motion (Figure 2*D* and *E*). She was able to swim and loosen up the shoulder. Her joints were painless, and x-rays showed bridging of the graft and early trabecular bone crossing the osteotomy site.

Dr. Ivins:

We obviously lost a lot of position at the operative site. Her arm did not look as bad as the x-ray indicates, however. The arm had an acceptable appearance. Would anyone care to comment about the initial treatment? Just forget the other extenuating circumstances, the stiff shoulder, and the elbow still in moderate extension.

Dr. Coventry:

The case speaks for itself. You succeeded. That is the best way to handle it.

Dr. Ivins:

I would not know how else to handle this case. By virtue of her other operation, she had a lot of scar tissue. There was not much to work with because of the short distal fragment. The short plate was mortised into the distal fragment, which accounted for some loss of firm fixation, and thus the angulation. But I actually think her loss of position, as evident on the x-rays, is more a product of our efforts to try to get motion back into her shoulder, elbow, and hand than anything else.

Dr. Dobyns:

How soon did you start her on active motion?

Dr. Ivins:

I do not know exactly, but about the end of the seventh week, I think.

Anthony J. Bianco, Jr., M.D.:

Initially, I would have treated it with a Velpeau dressing plus a collar and cuff.

Dr. Ivins:

I think that is a good form of treatment, assuming that you have a cooperative patient. She was a woman of very spare build. I think she could have been treated in many nonsurgical ways, by the immobilization you have just described or perhaps by a hanging cast or simply by a Velpeau dressing. I would have given it a try.

Dr. Bianco:

You would not have opened the fracture originally?

Dr. Ivins:

No, I would not have.

Dr. Fisher:

The question of order of treatment regarding the stiffness of the joints in trying to maintain or return some motion and general health to the extremity before treatment of nonunion is one that challenges everyone. That is why

this woman came to our clinic. Previously all efforts were made to restore motion of the wrist, hand, elbow, and shoulder before an effort to treat the nonunion was made.

Case 3

Dr. Fisher:

A 40-year-old fertilizer plant manager was in an automobile accident in October 1965. He suffered fractures of the shafts of both humeri. There were no other injuries. The right humeral-shaft fracture was treated with a Rush pin in the hope of gaining early motion and function. The left humeral fracture was treated by a hanging cast. As you might surmise, the left humerus healed completely in two months, while the right did not unite. Eleven months later, the nonunion was treated by removal of the rod, application of iliac grafts, and use of a long-arm cast for fixation. Fourteen months after fracture, a sliding bone plate and iliac grafts were done. The patient came to our clinic almost three years after his original injury, with good range of motion at the shoulder, arm, hand, and wrist. It was now 23 months since his last operation. He has now had three open attempts to gain union of this bone (Figure 3*A*).

Dr. Ivins:

What about the other humerus?

Dr. Fisher:

The left humerus healed very well and was stable in two months. Through the old lateral incision scar, the right humeral nonunion was exposed on November 14, 1968. The broken plate and four screws were removed. A pseudarthrosis was excised. The ends were again squared back to bleeding bone with a handsaw, and a six-hole compression plate with strips and chips of added iliac bone was used (Figure 3*B*). Velpeau dressings were used initially, and the patient went home in a long-arm cast.

Dr. Ivins:

Can anyone criticize the treatment? To summarize, there was no radial nerve palsy, the bone was exposed through the old scar of the patient's three previous operations, the pseudarthrosis was excised, the bone ends were

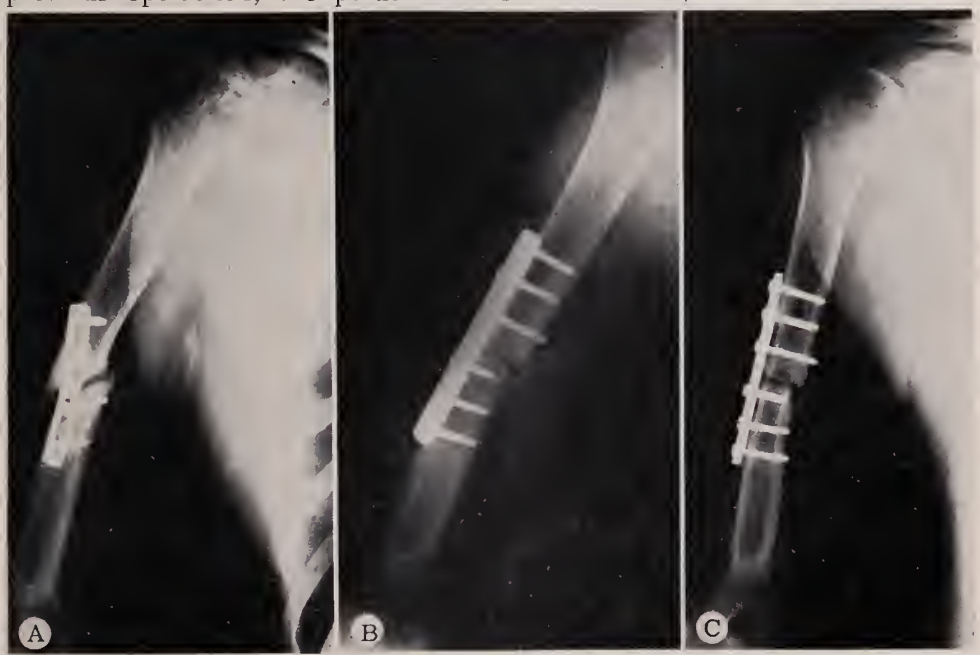


Fig. 3—(Case 3). *A*, Established nonunion and pseudarthrosis three years after fracture and three unsuccessful attempts at internal fixation. *B*, Postoperative excision of pseudarthrosis and compression fixation, with autogenous iliac bone grafts. *C*, Persistent nonunion five months after the fourth internal fixation.

squared off back to bleeding bone, and a six-hole compression plate was applied.

Dr. Coventry:

I would use a spica cast instead of a hanging cast.

Dr. Johnson:

How much shortening does this require, about 2 cm?

Dr. Ivins:

I would think almost 3 cm of total shortening.

Dr. Henderson:

I think that, if you are going to do open reduction and fixation of a fracture of the humerus, good internal fixation should be sufficient. The problem is that, in many cases, internal fixation is not adequate. I know of three patients who have been treated the same way for the same reason, and the results have been very successful. There is the problem of the compression plate. Does it really work because it supplies compression or because it is good internal fixation? Mechanically, these devices are made so that there is good, rigid internal fixation. I think that if you are going to do internal fixation, it must be good and rigid—this is the real problem.

Dr. Ivins:

In this situation, disregarding whether or not compression has any value, do you believe that a single, heavy six-hole plate gives adequate fixation?

Dr. Henderson:

I would feel a lot safer with two plates at right angles to each other.

Dr. Fisher:

The patient's x-ray was taken on April 23, 1969, five months after the compression plate was applied (Figure 3*C*). He had maintained good motion but still had pain.

Dr. Ivins:

He still had pain at the fracture site, and no evidence of union after five months.

Dr. Fisher:

Consultation with Dr. Ivins' colleagues was obtained, and opinions varied.

Dr. Ivins:

After four operations, the patient had a normal shoulder, elbow, wrist, and hand and normal fingers. He had no radial-nerve problem; the condition of his skin was good. He has had four operations and now has a six-hole plate and six screws, with evidence of nonunion that is more obvious now than it was in the early postoperative period. What should the next move be?

Dr. Henderson:

Is there a reaction around the screws?

Dr. Fisher:

I tried to trace any motion or any screw reaction through on the intervening x-rays and I could not see any. You can see how the humerus had been reamed distally before.

Dr. Coventry:

Right where the artery is, as you pointed out earlier, I would put in iliac onlay grafts medially and wait it out. I would not trust this plate and six

screws and osteoporotic bone to take care of all the torsional rotation forces. Dr. Henderson says that this is usually sufficient, but not always. My experience is somewhat different.

Dr. Ivins:

Are there any indications to remove the plate?

Dr. Coventry:

No. I would add onlay grafts.

Dr. Dobyns:

In orthopedic training, we spend most of our time discussing bone mechanics and mechanical stability of the fracture, which is important. But there are other things to think of. We should mention the soft-tissue environment, which I think is very important in the development of a nonunion. Maybe nobody agrees, but I think you need a nice, clean bed of soft tissue to adequately treat any nonunion by surgical means.

Dr. Ivins:

I agree. This is extremely important. By way of summary, I would like to mention the following points: (1) Often the least treatment produces the best results in fractures of the humeral shaft. (2) Open reduction should not be undertaken lightly and, if done, should be augmented by good, rigid internal fixation. (3) With proper treatment and good rehabilitation, the average closed humeral-shaft fracture should produce minimal disability.

John C. Ivins, M.D.*
Darrell E. Fisher, M.D.†
Einer W. Johnson, Jr., M.D.*
Rochester, Minnesota

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†Chief Resident Associate, Department of Orthopedics, Mayo Clinic and Mayo Foundation.

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One breaks your bones, one sets them in their sockets;
But vaccination certainly has been
*A kind of antithesis to Congreve's rockets,**
With which the Doctor paid off an old pox,
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*Sir William Congreve, inventor of improved artillery
†Lord Byron, **Don Juan**, Canto I, verse CXXIX. 1819.

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*Aristophanes' **The Clouds** (play from ancient Greece, 4th century BC).

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Continued on page 409

"The history of science, and in particular the history of medicine... is... the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

—George Sarton, from "The History of Medicine Versus the History of Art"

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Opinion & Dialogue

Dialog

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

Herbert L. Ley, Jr.,
M.D., M.P.H., Formerly
Commissioner, F.D.A.
(1968-1969)
Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations,



state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the public. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of what the medical community *and* federal regulators do will often be represented in simplistic and somewhat misleading terms.

One illustration of the misuse of the media in this regard is the recall of anticoagulant drugs several years ago. This FDA action was given publicity by the press and television that went far beyond its probable importance. The result was a very uncomfortable situation for the practitioner who had patients taking these medications. Since the practitioner and pharmacist had not been informed of the action by the time it was publicized, in most states they were deluged with calls from worried patients.

The practitioner can attempt to solve these problems of inadequate communication in several ways. One would be the creation of a communications line in state pharmacy societies. When drug regulation news is to be announced, the society could immediately distribute a message to every pharmacist in the state. The pharmacist, in turn, could notify the physicians in his local community so that he and the physician could be prepared to answer inquiries from patients. Another approach would be to use professional publications the practitioner receives.

All of this leads back to my opening contention: if drug regulation is to be effective, timely, and related to the realities of clinical practice, a better method of communication and feedback must be developed between the nongovernmental medical and scientific communities and the regulatory agency.

ue

Maker of Medicine

Henry W. Gadsden, Chairman & Chief Executive Officer, Merck & Co., Inc.



In my opinion, it is the responsibility of all physicians and medical scientists to take whatever steps they think are desirable in a law- and regulation-making process that can have far-reaching impact on the practice of medicine. Yet many events in the recent past indicate that this is not happening. For example, it is apparent from drug efficacy studies that the NAS/NRC panels gave little consideration to the evidence that could have been provided by practicing physicians.

There are several current developments that should increase the concern of practicing physicians about drug regulatory affairs. One is the proliferation of malpractice claims and litigation. Another is the effort by government to establish the relative efficacy of drugs. This implies that if a physician prescribes a drug other than the "established" drug of choice, he may be accused of practicing something less than first-class medicine. It would come perilously close to federal direction of how medicine should be practiced.

In order to minimize this kind of arbitrary federal action, a way must be found to give practitioners both voice and representation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

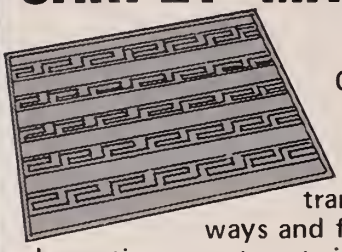
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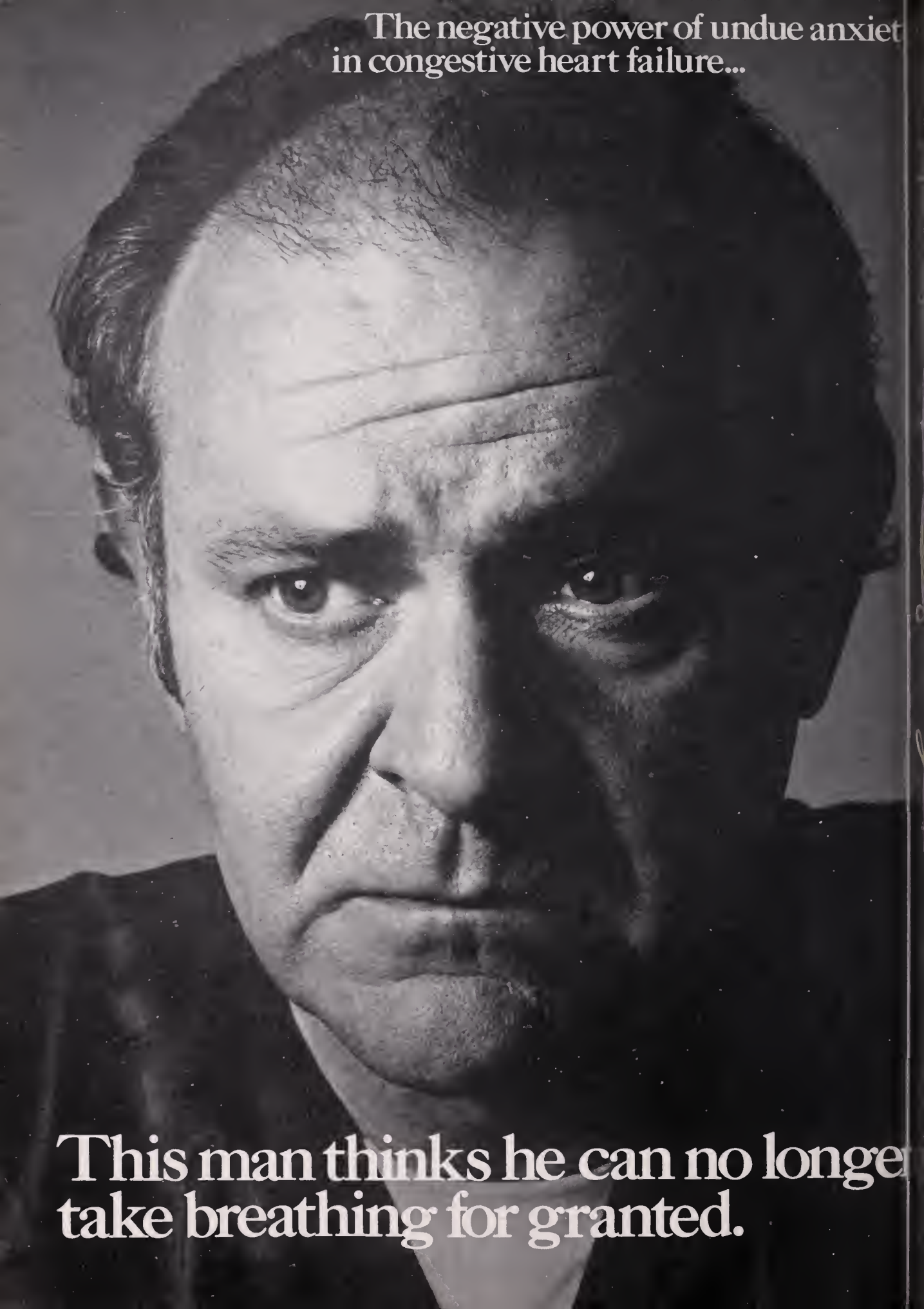
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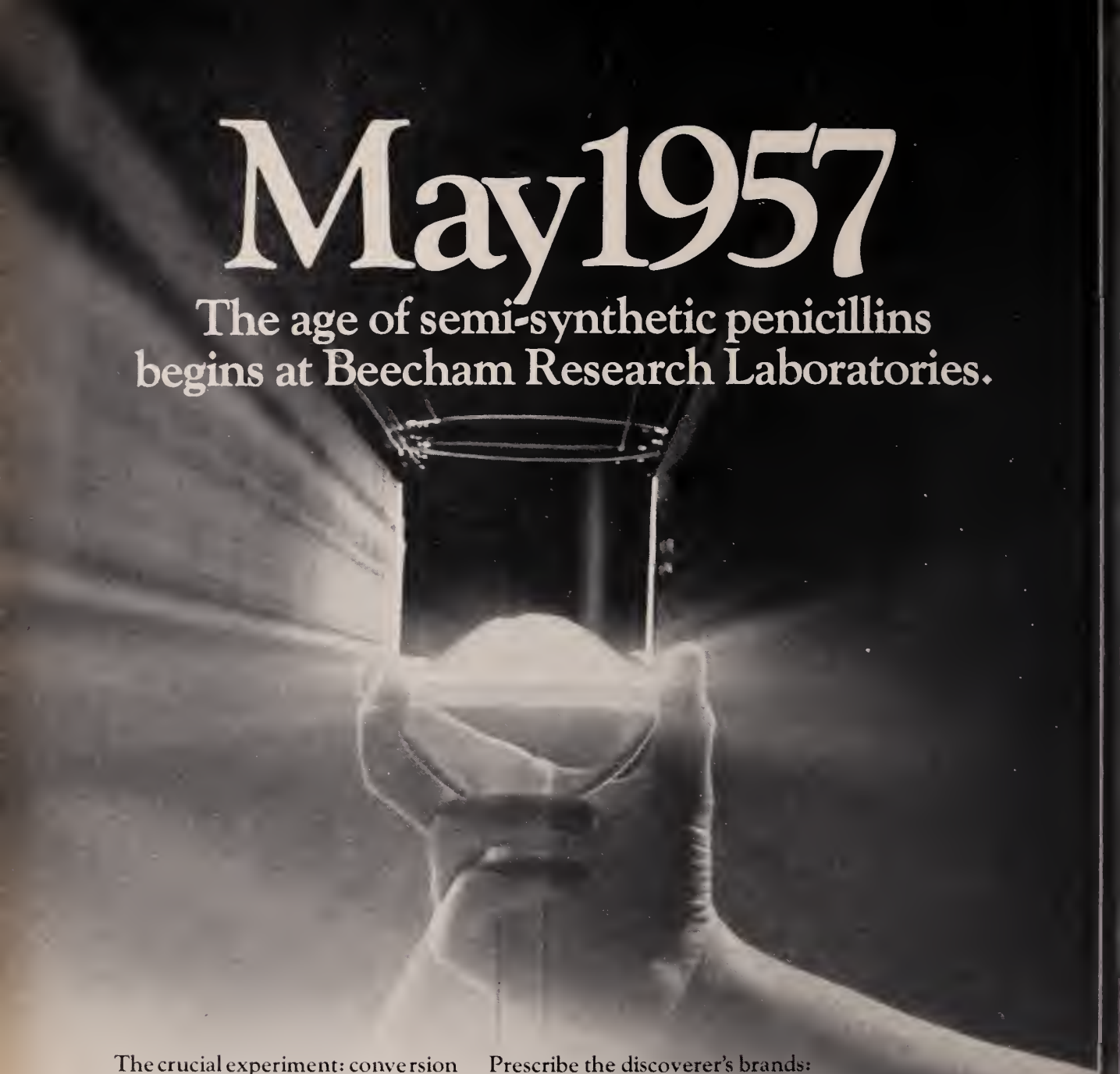
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Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®) may be of value if respiratory depression occurs.

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President's Letter

President's Report

THIS PAST YEAR has been both a challenging and rewarding year for me as President of The Minnesota State Medical Association. I have tried to visit as many component medical societies as possible to bring the State Medical Association closer to the Local Medical Society. In reviewing the past year, there were three significant developments.

1. As your president, I served on the Search Committee to recommend candidates for Dean of The Medical School on the main campus. Doctor Neal Gault was chosen. Doctor Gault is an excellent choice. I look forward to continued and improved communications between the medical school faculty and the community physician. I am sure that Doctor Gault has a good understanding of the problems and challenges that are involved in his new job; that he will be a conscientious and capable administrator.

2. The Physicians' Associate Program is emerging as a successful venture. Both the medical student and the community physician are enthusiastic in its support. This is the first program that has provided a year's training outside the Medical School. It has improved communications between the teaching physician and the Medical School. The faculty representative visits the medical student and his preceptor once monthly, and this provides educational opportunities for all the physicians in the community. I endorse this program and expect it to expand in the future.

3. Blue Shield has had many and varied problems for the past several years. For the past two years, Blue Cross has been providing administration and management to Blue Shield. In the past year there has been excellent communications between Richard Crist, the President of Blue Cross and Blue Shield, the Board of Directors of Blue Shield and the Council and officers of your State Medical Association. The meetings have been fruitful in defining and solving difficult problems. One month ago the Board of Directors of both Blue Cross and Blue Shield approved a total merger of the two companies. Ratification of this decision by the corporate bodies of both companies is expected. This will insure the solvency of Blue Shield. With this major development concluded, we can, through continued dialog, begin to solve the many remaining existing problems. This progress was made possible through the diligent work of the Administrative Staff and Board of Directors of both Blue Cross and Blue Shield. The patience and cooperation shown the doctors of Minnesota has been outstanding and with continued efforts, resolution of many existing problems will be accomplished.

I want to thank Harold Brunn and his staff for making my year so pleasant. They are really a great gang. Their efficiency is excellent and their spirit is great.

I want to congratulate Carl O. Rice for his untiring efforts for many years in behalf of MINNESOTA MEDICINE. I hope this issue is a fitting memorial to his efforts.

Robert T. Kelly

President
Minnesota State Medical Association



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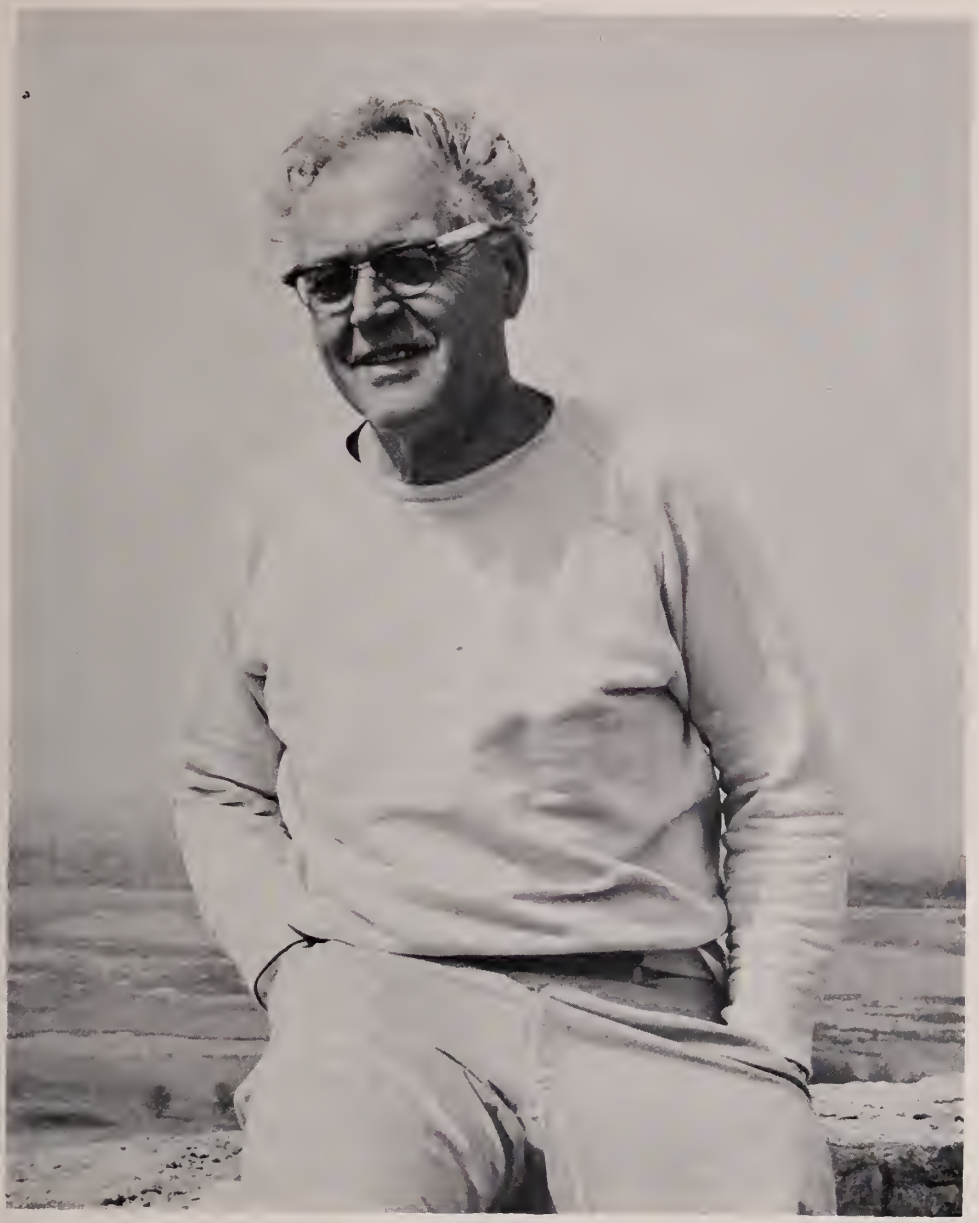
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Carl O. Rice, M.D.
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Carl O. Rice: Editor and Surgeon

"An editor is a surgeon . . . It is he who cuts thousands of words of dead wood, organizes and tightens, reshapes sentences, puts in the grammar and punctuation, and still retains the author's book too, though the author doubts it while the process is going on."—Helen K. Taylor, Editor, Viking Press

THIS IS A tribute to Carl O. Rice.

From 1961 through 1971 he served as Editor-in-Chief of MINNESOTA MEDICINE. He will continue as Editor Emeritus.

I have known Carl six years, long enough to appreciate him but not long enough to understand him, for Carl is a complex man. What I write here I learned from being his friend, working with him on the journal, reading his bibliography and interviewing him for this article.

Start of His Career

In 1929 Carl, three years out of medical school, became the first surgical resident of Owen Wangensteen. Early in residency, he saw a child with an imperforate anus. His problem was to find where the rectum ended. As he held the baby near the x-ray machine, a solution flashed through his mind.

Why not turn the infant upside down? Intestinal gas would rise. By placing a metal disc on the anal dimple, then measuring between gas and disc, he could tell exactly where the rectum ended. Later he and Doctor Wangensteen published this simple concept.[1]

This story gives insight into Carl's mind. He is a *why not* man. Because of this turn of mind he often turns problems upside down, converts conundrums into opportunities, and visualizes dimension others fail to grasp.

Contributions

From 1926 to 1929 Carl served as receiving officer at Hennepin County General Hospital. There he reduced many fractures. These reductions caused much pain. So Carl asked: *"Why not* inject procaine directly into the fracture?"

After two papers on the success of the method,[2,3] a well-known Boston orthopedic man, Doctor Cotton* came West to see a young physician's technique for painlessly reducing fractures.

From 1929 to 1933, while doing his residency (three years at the University of Minnesota, a year at Mayo's, then eight months as a fellow under Professor DeQuervain in Switzerland), Carl concentrated on thyroid disease. Again his original mind came into play. *Why not* look at *all* thyroid glands removed at *all* Twin Cities teaching hospitals—University Hospital, Minneapolis General, and Anker?[4] *Why not* use these specimens to study the "life cycle" of thyroid histology from youth to old age?[5] And in Switzerland, *why not* review a canton's experience with thyroid disease and compare it to Minnesota's?[6] So one thing led to another, and a spate of articles resulted.[7-13]

When Carl returned in 1934 to Minneapolis to practice he quickly learned surgeons do not live by thyroid surgery alone, so he focused on some practical aspects of the surgeon's craft.

One thing that annoyed him was the time required to thread needles in the operating room. He spoke about this to a representative of Ethicon. *Why not* make suture and needle a single functional unit? Indeed, *why not* make a series of these swaged needles—one round, one with a cutting edge, and one for intestinal anastomoses? Today millions of these 803, 805 and 123 Ethicon sutures are used throughout the world.

Postoperative deaths soon took his attention away from needles and sutures. Why did surgery go smoothly for patients, yet they died? The main problem, as he saw it, was postoperative-sustaining metabolism with the right mix of fluids, calories, and nitrogen-building compounds. To do this, a metabolism laboratory was needed. This was formed in 1942 at St. Barnabas Hospital. He would also need a flame photometer to measure electrolytes. This he got in 1948. And, of course, it would help to have a partner who understood such matters.

In 1950 Doctor Jacob Strickler joined him. They wrote a series of papers describing how they

*Trimalleolar fractures are often referred to as "Cotton's fracture."

developed electrolyte mixtures that achieved fluid balance, met caloric requirements, and led to a positive nitrogen balance.[14-24] Baxter Laboratories helped finance these studies and still market some of those fluid mixtures.

Through the years Carl has remained a technical innovator—a man with a different way of doing things. For example, he has described a muscle-splitting cholecystectomy incision;[25] a new approach for repairing hernias;[26] and a new procedure, "adenomammectomy", for removing benign breast lesions and hypertrophied breast tissue.[27]

Adenomammectomy

I shall dwell on the adenomammectomy procedure a moment because it reveals Carl's talents —both literary and technical. First of all, he coined the term "adenomammectomy"— a melliluous but precise word that said what he wanted to say. *Dorland's Medical Dictionary* first listed the word in 1966 and *Stedman's* followed in 1967.

Here's *Dorland's* version:

> "adenomammectory (ad" e - no - mah - mek' - to - me) *adeno - mamma - ektome* excision). Excision of part or all of the glandular tissue of the breast, leaving the fibrous capsule and the underlying skin and subcutaneous tissue."

I asked Doctor H. W. Heupel, Carl's other partner, what was different about this procedure when used as a reduction mammoplasty. He said the adenomammectomy concept showed how Doctor Rice thought three-dimensionally. Most surgeons, faced with a hypertrophied breast, would excise a generous segment of breast and skin, then pull together the remaining breast tissue to cover the defect, perhaps transplanting the nipple in the process. Not Carl. His concept is to remove the tissue from behind, "the base of the mountain", as Doctor Heupel says, thereby letting the breast settle back into its natural contour. A much simpler technique. Besides, the chances of the nipples being symmetrical are much greater. In any case, Doctor Ariel, prominent New York cancer surgeon, thought enough of the procedure to ask Doctors Rice and Strickler to contribute a chapter on it in the book *Progress in Clinical Cancer*.[28]

Writing and Editing

Up to this point, I have not commented on Carl's writing or editing. I shall do so now.

In writing, Carl believes strongly in four things: *Merit, Clarity, Flair,* and *Force.* In other words, if you have a nail to hit, pick a straight true nail, hit it on the head, hit it with style, and hit it hard.

For these reasons, Carl is a tough editor, one who cuts through the tangle to get at the pith. He likes to reduce the basic idea of an article into short sentences and short paragraphs, with subheadings to show the way.

This drive for clarity has resulted in editorial excellence. In 1967 the American Medical Writers Association named *Minnesota Medicine* as the best state medical journal. But his determination has ruffled some feathers too. Which is not surprising. For it is sometimes difficult to say: "Although this is a bad idea, it is also badly written."

As an editor, Carl has also been a gambling man. For instance he has placed his chips on colored cover photographs, betting on the reader's esthetic sense, and on foreign issues, risking that readers would enjoy worldwide contributors. Some gambles he has lost. But, true to character, he has never hedged his bets, nor has he made any side wagers.

I close with a quote from M. Lincoln Schuster, former president and Editor-in-Chief of Simon and Schuster, because I think it sums up Carl's feelings about his ten years as editor:

> "Editing can, and should be, not only a life-enhancing profession, but also a liberal education in itself, for it gives you a privilege of working with the most creative people of your time: authors, educators, world-movers, and world-shakers. For taking a lifetime course for which you would be willing to pay tuition, you are paid, not with dollars, but with intellectual and spiritual satisfactions immeasurable."

Richard L. Reece, M.D.
Minneapolis, Minnesota

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Metastatic Intestinal Kultschitzky-Cell Carcinoma (Carcinoid) Diagnosis of by Sternal Bone Marrow Biopsy

EMIL MARO SCHLEICHER, Ph.D.*, DENNIS J. KANE, M.D., Ph.D.† and H. WILHELM HEUPEL, M.D., Ph.D.‡

DEMONSTRATING METASTASES to the bone marrow of an intestinal Kultschitzky-cell carcinoma can be important. Yet, though metastases of this tumor to the marrow have been observed at necropsy, we are not aware of any instance where the diagnosis of metastasis was unequivocally established by sternal marrow biopsy as was the case here.

Case Report

A 59-year-old physical education teacher, was admitted to St. Barnabas Hospital§ on August 7, 1969. Eight months before she was plagued by intermittent explosive diarrhea and lost 24 pounds. For a month she experienced pain between the shoulder blades and in both flanks. She underwent a thyroidectomy 20 years before.

A slight exophthalmos was noted. The patient was emaciated and dehydrated. The abdomen was distended and tender. Bowel sounds were active. There was dullness in the right chest on percussion. Thoracentesis yielded two liters of milky fluid from the right chest cavity. No malignants cells were found.

An intravenous cholecystogram showed a normal gallbladder. A liver scan with Au^{198} was negative. X-ray studies revealed a lower mediastinal mass, prominent mucosal folds in the jejunum, and dilatation of the small bowel. A complete blood count, serum electrolytes, and routine blood chemistry were not remarkable. The serum uric acid was 3.2 mg. percent, and the thyroxine chromatography level 5 mg. percent.

Malignant lymphoma was considered the likely diagnosis.

Because lymphocytic tumors may affect the marrow, a sternal marrow aspiration biopsy was done. This showed metastatic Kultschitzky-cell carcinoma. A laparotomy was performed. A tumor partially obstructed the lower jejunum. The bowel loop containing the primary tumor was fused to a mass over the aorta and vena cava. A jejuno-jejunostomy was performed. Yellow metastases, two to ten millimeters in diameter, studded the liver. These proved to be metastases of a Kultschitzky-cell carcinoma (carcinoid).

The patient received a course of L-phenylalanine mustard (Alkeran) and Prednisone one month after surgery. She died on October 11, 1969 from peritonitis due to gangrene of the invaded small bowel loop. Necropsy showed systemic metastases. Marrow from several sites disclosed metastatic tumor.

Sternal Marrow Biopsy

From the body of the sternum at the level of the second intercostal space, 10 ml. of marrow substance were obtained. One hundred marrow units were separated from the aspirate. The units ranged in size from 0.1 to 1.0 millimeter, and all were of the floating type. Marrow units are anatomical-physiological entities of the marrow organ, and can be individually affected by disease.[1] They were fixed in formolsaline fluid, embedded in paraffin, and serially sectioned, 5 micra thin. Stained with hematoxylin-eosin, the sections were then examined under the light microscope.

Metastatic tumor was detected in one marrow unit.

The tumor consisted of closely packed uniform polyhedral nuclei imbedded in an eosinophilic granular cytoplasm. A lighter staining bar-like area suggesting poorly formed glandular lumina was present within the nodular mass. Figure 1 shows the characteristic histopathology of the tumor in serial section #28. In serial section #39 the tumor presented a distinct glandular structure. The acinus contained a small amount of inspissated amorphous eosinophilic material. (Figure 2).

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#The spelling of Kultschitzky's name varies as he was a Russian and probably used Cyrillic lettering. We have adopted R. A. Willis' spelling as authoritative.
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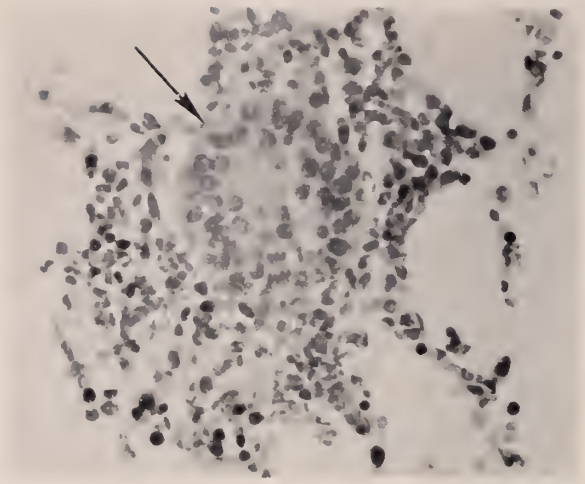


Fig. 1—Section; 5 micra thick of the single marrow unit with tumor metastasis. Arrow points at the solid nodular growth. The histopathology is characteristic of Kultschitzky-cell carcinoma (carcinoid). Hematoxylin-Eosin; x 190.

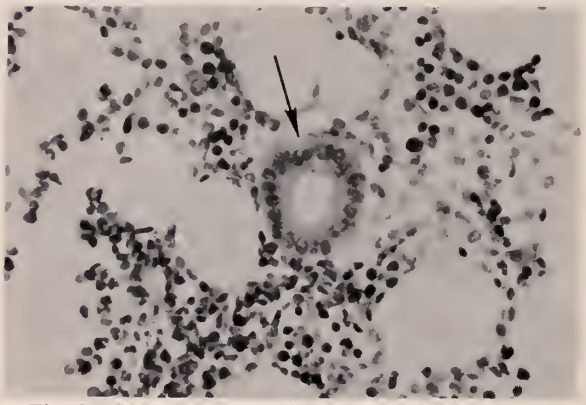


Fig. 2—Same marrow unit as Fig. 1. Arrow points at the glandular structure of the metastasis. Hematoxylin-Eosin; x 190.

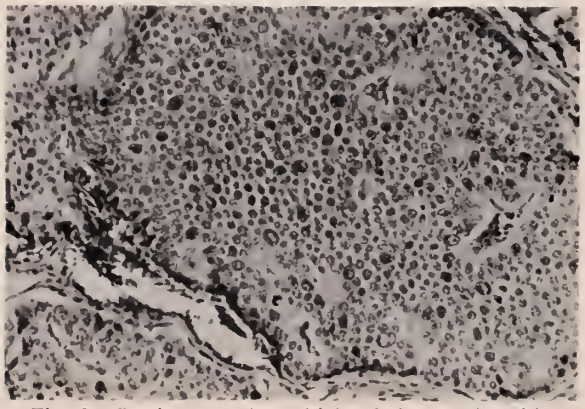


Fig. 3—Section; 5 micra thick of the surgical biopsy of the intestinal tumor. Hematoxylin-Eosin; x 75.

This lesion was interpreted as a metastasis of a Kultschitzky-cell carcinoma (carcinoid).

Figure 3 shows the histopathology of the intestinal tumor, obtained at surgery.

Discussion

Willis[2] does not like the term "carcinoid tumor" because it implies innocence. Carcinoids, especially of the small intestine, can invade and metastasize. Because the tumor arises from the yellow cells of Kultschitzky situated in the crypts of Lieberkuhn, the tumor should be called argentaffin or Kultschitzky-cell carcinoma. In most cases the histopathology of, the tumor is distinct, and identification usually offers no difficulties. The Kultschitzky-cell carcinoma is made up of well defined solid sheets or strands of small closely packed polyhedral cells, with small glandular lumina or distinct acini scattered through the tumor. The more actively growing tumors show various degrees of anaplasia and may escape recognition.

Speirs and Williams[3] advocate resection of the primary tumor if feasible. They conclude, "The prognosis of multiple carcinoid tumors of the small bowel wtih mesenteric metastases remains guarded but seems much more favorable than other types of small bowel malignancy with metastases."

Metastasis to the marrow organ indeed connotes hopelessness in most cancers, but a favorable response to surgery and chemotherapy can at times be hoped for in Kultschitzky-cell carcinomas. Even if bone marrow metastases are found in this tumor, the case for palliative resection and chemotherapy can be argued.

Summary

A Kultschitzky-cell carcinoma of the small bowel was first diagnosed by bone marrow biopsy in a 59-year-old woman. To our knowledge, this has not been reported previously. This tumor responds at times to surgical and medical treatment. Its detection in bone marrow biopsy can be of prognostic and therapeutic consequence.

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Granulomatous Peritonitis Induced by Cornstarch Powder

JOHN R. HORNUNG, M.D.* AND ARNOLD J. KREMEN, M.D.*

SINCE THE INTRODUCTION of the rubber glove to surgery, hand powders have accompanied their use in the operating room. Numerous papers documenting iatrogenic disease resulting from these powders in the abdominal cavity have been reported. Two additional cases will be presented.

Case Report

On February 23, 1971, a 43-year-old, white female with symptoms of chronic cholecystitis underwent a cholecystectomy, operative cholangiogram and an appendectomy. At that time exploration of the abdomen was negative. Her postoperative course was uneventful and she left the hospital on the tenth postoperative day. A T-tube was not used.

Subsequent Progress

Four weeks after her surgery she noted the gradual onset of lower abdominal aching pain, more marked on the right. She had several episodes of fever and chills. She denied nausea, vomiting, diarrhea or constipation. She had no urinary symptoms and her menstrual periods were normal. The symptoms persisted and she was readmitted to the hospital on March 31, 1971.

Physical findings revealed marked tenderness to palpation in the lower abdomen, marked rebound tenderness, the suggestion of a mass in the right lower quadrant. Pelvic examination revealed tenderness in the cul-de-sac and in both adnexa. Manipulation of the cervix caused pain.

The initial diagnostic impressions were pelvic inflammatory disease, possibly diverticulitis or granuloma of the cecum subsequent to her appendectomy.

Laboratory Examination

Hgb. 14.0, WBC 10,300 with 74 neutrophils to 12,500 with 79 neutrophils and six eosinophils, sedimentation rate 56 → 80, Na, Cl, K, HCO_3, urinalysis, serum proteins, Ca + +, PO_4, cholesterol, glucose, BUN, creatinine, uric acid, bilirubin, alkaline phosphatese, LDH and SGOT normal. Electrocardiogram was normal. Chest and abdominal films were also normal. Barium enema revealed a concave defect medially and inferiorly in the cecum; there were no diverticuli. A culdocentesis revealed clear fluid, mesothelial cells and a mixed inflammatory infiltrate with moderate numbers of neutrophils; culture of this fluid was sterile. Cultures of urine and blood were also sterile and cervical cultures were negative for N. gonorrhoeae.

Hospital Course

Due to the impression that her symptoms and findings were secondary to an inflammatory process, she was treated nonoperatively with large doses of antibiotics. For two weeks her temperature ranged between 99 and 101 F. and she had several episodes of chilling. During this time she was able to eat, there was no vomiting and she passed gas and stool by rectum. Nevertheless, her fever persisted and she continued to have pain and tenderness and the suspicion of a diffuse mass in the lower abdomen persisted. In view of her failure to improve she was again operated upon on April 15, 1971.

Findings at Operation

Upon entering the peritoneal cavity, an enlarged, beefy, thickened, and indurated greater omentum was seen intimately attached to the cecum on the right and to the sigmoid colon on the left. In the pelvis it was densely adherent to the uterus, ovaries and tubes. Small bowel, including terminal ileum, was adherent to the under surface of the omentum, but, surprisingly, appeared otherwise normal. There was approximately one liter of straw-colored ascitic fluid in the abdominal cavity. There were no miliary granulomas on the seroseal and peritoneal surfaces. Tissue specimens from the omentum and peritoneal surfaces revealed marked subacute in-

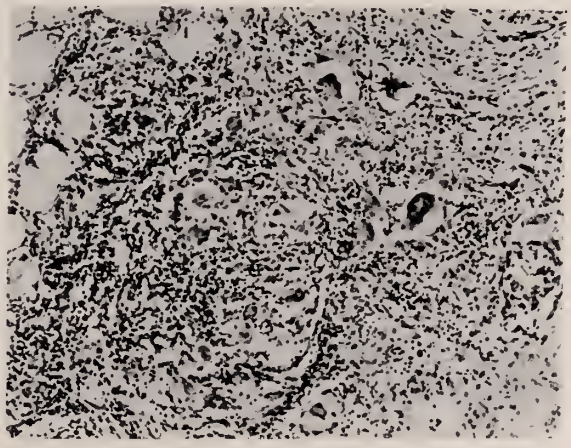


Fig. 1—H/E section (x) showing chronic inflammatory and foreign body giant cell reaction in fat.

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See editorial, page 455.

flammation with many eosinophils, numerous foreign body giant cells and some doubly refractile material. The pathologists' conclusion was that this represented a granulomatous reaction with foreign body giant cell reaction to doubly refractile material (Figures 1 and 2).

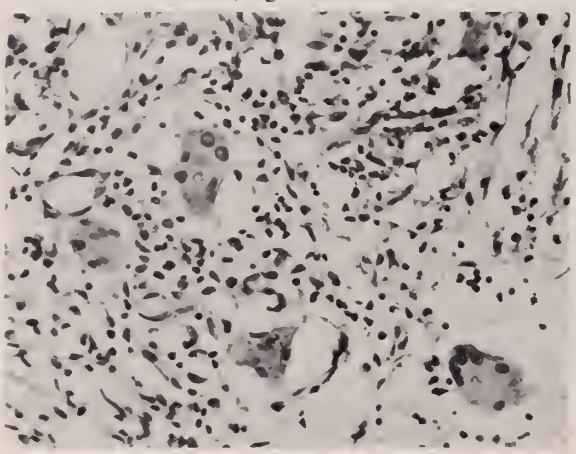


Fig. 2—H/E section (0x) showing crystalline inclusions in giant cells.

Another similar case showed thickened, indurated and inflamed greater omentum densely adherent to the peritoneum of the anterior abdominal wall and the serosa of the underlying small bowel. Approximately 1,000 cc. of straw-colored ascitic fluid were present. Frozen sections of several biopsy specimens revealed foreign body granuloma. Study of the permanent sections demonstrated doubly refractile particles in the granulomas consistent with starch powder.

Discussion

In 1916, Shatlock described a granuloma due to "silicious particles." From 1933 to 1947 many reports pointed out the potential hazards of talc when deposited in the abdominal cavity. Lee and Lehman[1] instilled one gram of cornstarch powder into the abdominal cavities of each of 10 dogs and found it to be completely absorbed without significant reaction three weeks after operation. One gram is the equivalent of that found on eight pairs of surgical gloves.

Lee[2] demonstrated that, although treated starch powder is biologically absorbable in tissue, it produces a foreign body reaction as long as it is present. The intensity, duration and reversibility of the reaction is influenced by (1) the dispersion of the powder, (2) the presence of infection or malignancy, (3) the individual hypersensitivity to cornstarch.

Sterilized cornstarch powder, Bio-Sorb, was considered superior to talc as a lubricant for surgical gloves, if precautions were taken to prevent powder contamination of open wounds and serosal surfaces, and became accepted in most surgical centers throughout the world.

Although laboratory work had demonstrated the irritative effects of starch powder, no reports of foreign body reactions in humans had been reported until 1955. Sneierson[3] reported a patient who, one month following nephrectomy for carcinoma, developed fever, chills and a fluctuant mass in the abdomen. Re-operation demonstrated foreign body granulomas due to starch powder.

McAdams[4] pointed out that "cornstarch, although absorbable, constitutes as much a foreign body as any other powder of comparable size until absorbed. The completeness of absorption and the time necessary for its accomplishment is dependent on the presence or absence of all factors conducive to inflammatory reaction." He reported five cases.

Maggs,[5] Myers,[6] Webb,[7] McNaught,[8] Hyden,[9] Taft[10] and Bates[11] have reported similar cases. The age of the patients ranged between 27 and 70 years. The time interval between initial procedure and onset of symptoms was 15 day to five and one-half weeks. Pain was steady or crampy and most often associated with tenderness not necessarily localized to the area of previous surgery. In one-half of the cases there was a low grade to moderate fever. Nausea, vomiting and obstruction were not found in all cases. The gross pathology revealed (1) copious amounts of straw-colored ascitic fluid; (2) one to three millimeter miliary granulomas covering the peritoneal and serosal surfaces; (3) multiple dense adhesions. Microscopic pathology always revealed chronic inflammation with granulomas consisting of giant cells, epithelioid cells, macrophages, lymphocytes and eosinophils. Starch granules appear red with acid-Schiff stain, and under polarized light are birefringent and show Maltese crosses. The prognosis is usually excellent. Most patients recover immediately, others have a low grade fever with pain for several weeks. One patient died of a subphrenic abscess resulting from his second exploration.

Conclusions

The relative paucity of reported cases of this

latrogenic granulomatous peritonitis is probably due to non-recogntion. Many cases of postoperative crampy pain and intra-abdominal distress may be due to this process. Rinsing one's hands in saline is inadequate for the removal of starch powder from surgical gloves. Scrupulous care in wiping away all residual powder from the gloves with a moist towel is recommended.

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It's the Law

Disability Benefits Terminated for Refusal to Undergo Surgery

A 37-year-old ambulance driver sustained a ruptured spinal disc. He was unable to continue working and began receiving disability benefits. He was examined by ten physicians and orthopedic surgeons. His back pain persisted and laminectomy was recommended on numerous occasions. Despite these recommendations the patient refused to undergo surgery and after three years of treatment the Social Security Administration terminated the man's disability benefits.

According to the law anyone who willfully fails to follow prescribed treatment without justifiable cause cannot be found to be under a disability.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Barnes v. Richardson, 320 F. Supp. 1267 (D.C., Ore., Dec. 22, 1970).

It is not while beauty and youth are thine own,
And thy cheeks unprofan'd by a tear,
That the fervour and faith of a soul can be known,
To which time will but make thee more dear;
No, the heart that has truly lov'd never forgets,
But as truly loves on to the close,
As the sunflower turns on her god, when he sets,
*The same look which she turn'd when he rose.**

*Thomas Moore's: Believe Me, If All Those Endearing Young Charms.

Aorto-Iliac Disease*

EDWARD G. ROCKWELL, JR., M.D.†

The aorto-iliac area is a common site for occlusive disease. Atherosclerotic deposits often become rather far advanced before symptoms appear, due to the large size of the vessels and the tendency for collateral to develop. Diagnosis can be made on physical examination, by decreased or absent femoral pulses. Disabling claudication is the typical operative indication.

Aortography is a useful guide to the management of these patients, not only showing the aorto-iliac area but the collateral and runoff as well, in many cases. Bypass grafting is the procedure of choice in most cases, as diffuse involvement is the usual finding. Endarterectomy is most suitable for localized involvement of the bifurcation area.

THIRTY YEARS AGO, Leriche described a syndrome which was due to atherosclerotic occlusion of the distal aorta. In his initial series, of male patients concentrated in the 50- to 60-year age group, symptoms of lower extremity fatigue, weakness, and atrophy, were associated with an inability to maintain a penile erection.[1]

The symptom of claudication is much more common than the weakness and atrophy emphasized by Leriche. While classically the pain is in the buttocks, hips, and thighs, a significant number of patients also complain of calf claudication. The calf may actually be the more common site of pain.[2-4]

Alterations in sex function are by no means a constant finding: they may be lacking in the most severe cases and often go unrelieved in spite of successful arterial surgery. In one series, a third of the patients with inability to sustain an erection were improved by surgery, but an equal percentage, normal in this respect preoperatively, complained of the loss of erection following surgery.[5]

The Patients

Most of the patients with aorto-iliac occlusive disease are males in their mid to late 50's, some years younger than patients with femoropopliteal disease. Table 1 gives some idea of average ages and male-female percentages in different series.[6-14]

A significant number of patients have high blood pressure, coronary artery disease, and cerebrovascular disease as shown in Table 2[15-18]

On physical examination there are decreased or absent femoral pulses, with bruits heard over the distal aorta, iliac, and femoral arteries, if the iliac arteries are not completely occluded. An occasional patient without femoral pulses will have popliteal and pedal pulses, due to collateral flow into the deep femoral system.

Usually the lower extremities are normal in color and warmth. There is little or no hair loss, skin atrophy, or muscle wasting. A minority of patients will present with these changes, however, and occasionally have ulceration or gangrene as well.

TABLE 1

Aorto-Iliac Disease
Average Age of Patients
Male/Female Percentages

Author (Year)	No. Pts.	Av. Age	Males (%)	Female (%)
Massarelli (1967)	105	55	87	13
Shepherd (1960)	52	53	87	13
Whitman (1962)	80	51	80	20
Dickinson (1967)	100	64	83	17
Gaspar (1967)	127	55	71	29
Gomes (1967)	411	53	80	20
Buckberg (1968)	150	55	66	34
Moore (1968)	58	62	100	
Renwick (1969)	40	56	87	13

*Presented at the Big Mountain Medical-Ski Conference, Whitefish, Montana, January 28, 1970.

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Criteria for Surgery

The small but real risks of arterial surgery do not justify the treatment of asymptomatic or mildlysymptomatic patients. However, claudication significant enough to interfere with the pationt's livelihood or ability to enjoy life is a reason for surgical treatment.

Rest pain, ulceration, and impending or actual gangrene represent rather urgent indications for treatment, as they suggest severe limb ischemia. Table 3 gives an idea of the indications for surgery in various series.

The Role of Aortography

Translumbar aortography was introduced by DosSantos in 1929.[19] It remains the method of choice in the angiographic evaluation of the patient with aorto-iliac occlusive disease, and can be a useful guide to operative management. It may show an unexpected aneurysm or renal artery stenosis which deserves treatment at the time of surgery. By proper timing of the second or "delayed" film, outflow can often be evaluated in the femoral segment, if the iliac arteries are open. If there is a question concerning the adequacy of the runoff, it can be studied directly by femoral arteriography.

Several surgeons have popularized translumbar aortography and have demonstrated its value and relative safety. DeBakey reported over 5,000 cases by 1966, with only two significant complications.[20]

On the other hand, aortography has been regarded by some surgeons as unnecessary. Edwards for example, believes that hypertension is the only indiciation for aortography, to determine if renal artery stenosis is present. If so, this will be corrected with the aorto-iliac disease.[21]

History of Surgical Treatment

Leriche in 1940 suggested removal of the aortic bifurcation along with lumbar sympathectomy in order to prevent propagation of thrombus and "vasoconstrictor reflexes." As grafts were not available at that time, collaterals were relied upon for lower limb survival.

The first endarterectomy was reported in 1947.[22] In 1951, Julian in the U.S. and Oudot in France described resection of the bifurcation with homograft replacement.[23-24] Degenerative changes and aneurysm formation have since made homografts outdated. As their use declined, interest developed in synthetic or prosthetic graft materials. Vinyon "N" was reported in 1952, and orlon, in 1956.[25-26] A year later, dacron and nylon were introduced, and they remain the most popular.[27-28]

In patients with severe unilateral iliac disease, whose general condition precludes a major operation, a bypass may be performed under local

TABLE 2
Aorto-Iliac Disease
Incidence of Associated High B.P., Coronary Artery and Cerebrovascular Disease

Author (Year)	No. Pts.	High B.P.	Cor. A. Dis.	Cerebro. Vas. Dis.
Beckwith (1958)	65	49%	75%	21%
Darling (1964)	137	....	80	5
Dickinson (1967)	100	33	19	3
Gomes (1967)	411	38	31	4
Buckberg (1968)	150	15	17	7
Minken (1968)	211	31	36	4
Humphries (1969)	331	8	25	8

TABLE 3
Aorto-Iliac Disease
Indications for Operation

Author (Year)	No. Pts	Claudicat.	Rest Pain, Ulcerat., Gangrene	Other
Darling (1964)	137	60%	40%	
Dickinson (1967)	100	74	26	
Gaspar (1967)	127	72	25	3%
Gomes (1967)	41	49	51	
Buckberg (1968)	150	85	15	
Minken (1968)	211	64	36	
Humphries (1969)	331	58	42	

anesthesia. In 1962 Vetto popularized the femoro-femoral bypass, bringing the graft subcutaneously over the pubis from one leg to the other.[29] Blaisdell introduced the axillary-femoral bypass in 1963.[30]

Subsequently Sobel has demonstrated the efficacy of CO_2 gas under pressure in separating the atherosclerotic intima and media from the outer vessel wall.[31] This method allows the removal of a solid "core" of material, including extensions into the mouths of branching vessels, and is effective over a several centimeter distance.

The More Common Methods of Treatment

With endarterectomy, or removal of the atheromatous material, the surgeon has to find the right plane of dissection, and he has to leave a smooth surface. A gradual distal taper or careful "tacking down" of remaining intima at the point where the endarterectomy is terminated is important, because a leading edge will elevate into the lumen and obstruct. If common femoral endarterectomy is necessary, it is done so as to direct blood into the deep femoral artery, which is rarely diseased beyond its proximal few centimeters.

Endarterectomy of diffuse disease—reaching into the external iliac or femoral arteries—is time consuming and tedious: however, it does offer the advantage of restoring patency without leaving a foreign material such as a graft. It is ideally suited for localized lesions of the bifurcation.

The other common method of treatment is bypass grafting; this allows correction of obstruction with the least dissection and time. Grafts are secured to the anterior walls of vessels, which tend to be less diseased than posterior walls. Proximally, the graft is placed midway between the renal arteries and the inferior mesenteric artery, where the aorta is usually of good quality. An occasional thrombectomy may be necessary at this level, but endarterectomy is usually not.

If there is localized aorto-iliac involvement, the graft is carried distally to the external iliacs. If these arteries appear significantly diseased, the graft is taken to the common femoral arteries. As in endarterectomy, emphasis is placed on revascularizing the limb through the deep femoral artery, if the superficial femoral is occluded or stenosed.

A third method of treatment is resection and graft replacement. This is necessary when an aneurysm accompanies occlusive disease, or when calcification of the aortic and iliac walls makes suturing impossible.

The Results of Surgery

It is very difficult to compare different procedures when they are used under different circumstances. While some surgeons use endarterectomy almost exclusively, and others prefer grafting, in many centers bypass grafting tends to be used in patients with more diffuse disease, because it is quicker and less technically demanding. Endarterectomy tends to be used in more localized disease of the bifurcation. Because these two procedures are used in different circumstances, for different degrees of disease, it is misleading to compare them.

Although it has not been proven, bypassed patients may have more coronary and cerebral atherosclerosis than those with localized aorto-iliac disease, thereby increasing operative mortality. Likewise, if bypassed patients have more diffuse disease, including femoral and popliteal vessels, this compromised outflow is apt to lead to failure of aorto-iliac reconstruction. Statistics suggest this relationship.

There are difficulties not only in comparing procedures, but also in arriving at an exact definition of results. Some surgeons use the life table method, which determines results at yearly intervals. On the other hand, so-called "early and late patency rates" used by others do not use exact time intervals: "early" patency referring to patency when the patient is discharged from the hospital, and "late" patency referring to whenever a follow-up study is done, including all discharged patients, at different postoperative intervals, in one group. Obviously, in evaluating results, it is important to know how percentages are determined. Often, this is not well defined. Realizing these difficulties, some different series can be examined.

TABLE 4
Aorto-Iliac Disease
Surgical Treatment
234 Cases

Bypass Graft	(119)	50%
Endarterectomy	(92)	40%
Combination	(23)	10%
Overall Early Patency		85%
Graft	(80%)	
Endarterectomy	(92%)	
Combined	(86%)	
Overall Late Patency		77%
Graft	(66%)	
Endarterectomy	(79%)	

In Table 4, the University of Rochester experience (Minken et al.), shows superior early and late patency rates for endarterectomized patients. However, endarterectomy tends to be used in more localized (and, therefore, more favorable) disease: in particular 48 of 90 endarterectomized patients had unilateral iliac disease.

Table 5 reviews the Baylor University experience. Most of the patients were bypass grafted although graft and endarterectomy results are grouped.[32] Late patency was 94% in a more recent survey from Baylor, with the number of patients then exceeding 3,000.[33]

TABLE 5
Aorto-Iliac Disease
2,029 Patients
1,306 Cases—Bypass Graft
179 Cases—Endarterectomy
544 Cases—Resection with Graft
Late Patency in 1,955 Cases (95%)

In Table 6, an English series (Dickenson, McNeil, and Morrison) superior patency rate for bypass grafted patients contrasts with results in other series.

Table 7 shows the Barnes Hospital results.[34] While endarterectomy had early superiority, this form of repair continued to occlude, so that at five years, patency rates were essentially equal.

Attempting to reconcile results from different authors, a compilation of late patency rates by author and year, in some larger series, is shown in Table 8.

Complications of Surgery

Thrombosis in the immediate postoperative period is the most frequent and significant complication of surgery, whether bypass grafting or endarterectomy is used. The incidence of this problem in a few different series is shown in Table 9.

Various factors have been incriminated in the etiology of early thrombosis. In the analysis of nine cases shown in Table 10 (Buckberg et al.), obviously more than one factor was present in several cases. It can be seen that poor runoff, or distal disease, was the main one.

Mortality in a few series is shown in Table 11. Rates are definitely higher for the grafted patients, due to their being greater operative risks, with more diffuse disease.

TABLE 6
Aorto-Iliac Disease
100 Cases

Endarterectomy	63
Bypass Graft	29
Endarterectomy & Graft	8

Early Patency Rates

	%
Endarterectomy	82
Bypass Graft	92
Endarterectomy & Graft	75

TABLE 7
Aorto-Iliac Disease
216 Cases

	2 Yr. Patency	5 Yr. Patency
Endarterectomy (159)	81%	63%
Bypass Graft (57)	62%	62%

TABLE 8
Aorto-Iliac Disease
Late Patency Rates

Author (Year)	No. Cases	Procedure: Graft	Procedure: Endarterectomy
DeBakey (1966)	3,000	94%	
Gomes 1967)	411	72%	83%
Gasper (1967)	127		95.7
Dickinson (1967)	100	92	82
Buckberg (1968)	150		91
Kouchoukas (1968)	216	62	63
Minken (1968)	211	66	79
Humphries (1969)	331		75

TABLE 9
Aorto-Iliac Disease
Eariy Postoperative Thrombosis

Author	Year	No. Pts.	No. Thromboses	%
Buckberg	1968	150	9	6
Clarke	1969	61	7	11
Gaspar	1967	127	7	6.3
Gomes	1967	411	26	3
Humphries	1969	496	48	9.7

TABLE 10
Aorto-Iliac Disease
Early Postoperative Thrombosis

Poor outflow	9
Incomplete endarterectomy	5
Postoperative hypotension	3
Unsecured distal intima	1
Failure to use heparin at surgery	1

TABLE 11
Aorto-Iliac Disease
Surgical Mortality

Author	Year	No. Pts.	Procedure	Deaths	%
Buckberg	1968	150	Endarterectomy	5	3.3
Clarke	1969	61	Endarterectomy	5	8.0
Darling	1964	137	Endarterectomy	3	2.2
Gaspar	1967	127	Endarterectomy	6	4.7
Dickinson	1967	63	Endarterectomy	3	4.8
		29	Bypass graft	4	13.8
Gomes	1967	75	Endarterectomy	3	4.0
		288	Bypass graft	9	3.9
Kouchoukas	1968	159	Endarterectomy	11	6.9
		57	Bypass graft	10	17.5
Minken	1968	92	Endarterectomy	4	4.3
		119	Bypass graft	15	12.6

Influence of Femoro-Popliteal Disease

In four different series (Table 12) the authors divided the cases into groups, depending on whether or not femoro-popliteal disease was also present. Most of these represented superficial femoral occlusion. It can be seen that significant femoro-popliteal disease will affect the results of aorto-iliac reconstruction. The majority of patients will still be relieved of their symptoms if the limb is revascularized through the deep femoral system, carrying the graft or endarterectomy to the common femoral artery at the deep femoral takeoff. Only a small percentage of patients require a subsequent femoro-popliteal bypass if this is done.

TABLE 12
Influence of Femoro-Popliteal Disease
On
Aorto-Iliac Reconstruction

Author	Year	Patency With F-P Dis.	Patency Without F-P Dis.
Cannon	1961	68%	97%
Stokes	1963	64	82
Dyde	1968	68	89
Kouchoukas	1968	60	81

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15.-34. See page 474.

Nuclear Medicine

Current Concepts

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RICHARD A. PONTO, B.A.

THE PRACTICE OF Nuclear Medicine relates to the development, evaluation and propagation of various uses of radioactive materials in the diagnosis and treatment of disease. To this end, consideration is given to the availability of radioactive materials, to the availability and performance of devices for measurement of radioactivity, to a clinical evaluation of procedures performed and to the radiation hazards to patients and clinic personnel.

The initial use of radioactive materials in medicine followed shortly after the discovery of radioactivity by Becquerel in 1896. Following World War II, there has been a steady increase in the availability of reactor-produced radioactive materials so that today there are several hundred radionuclide preparations available for use in medicine and medical research. There is little doubt that the number of these radiopharmaceuticals will be increased substantially in the future with emphasis on those which have either a very short† physical or biological half-life or both and will permit the administration of quantities of radioactivity to patients with only a few millirads[1] of radiation exposures.

Radioisotopes

The rapid growth and availability of radioisotopes has been paralleled by similar advances in nuclear instrumentation. The sensitivity of nuclear instruments, together with physical properties of the radioisotope used (half-life, types of emissions) governs the radiation exposure to patients and personnel.

Instruments

A wide variety of instruments are available for use in Nuclear Medicine, all of which have some means of detecting and recording radioactivity, and, all of which employ a scintillation crystal detector coupled with a spectrometer for analysis of gamma ray energies of the radionuclides being used. Beyond this, instruments differ depending upon their particular application: for assay of radioactivity a scaler is generally used; if information is desired on the rate of uptake and clearance of a radioisotope from an organ, such as in studying the function of a renal transplant, then a rate meter and strip chart recorder are usually employed; images (scintiphotograms) of body organs containing radioactivity are obtained using a rectilinear scanner or scintillation camera. The camera is an instrument of relatively recent design and is used for studies in which dynamic function data are desired in addition to scintiphotograms. There appears to be little doubt that future developments in camera systems will provide significant improvement in resolution of scintiphotograms so that they will begin to approach the image quality currently available in conventional radiographic procedures.

Computer

With the aid of computer analysis, currently an integral part of many of the diagnostic procedures in Nuclear Medicine practice, quantitative information can be obtained relative to regional function and blood flow in a variety of body organs. A summary of these and other Nuclear Medicine procedures are listed in five categories in the Table.

Nuclear Medicine must employ the special talents of physicians in nearly all clinical specialties as well as researchers in the basic medical sciences, in order to carry out an effective and expanding program.

Case Reports

Lung Study

An example of a radionuclide lung examination is shown in the following case study on a 61-year-old patient

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†Seconds to minutes.

with progressive dyspnea. Selected scintiphotograms from the radionuclide studies show several areas of decreased perfusion in the lung (Figure 1). This pattern might also be seen in studies of patients with multiple pulmonary emboli. However, the scintiphoto obtained following a single breath of 133-Xenon (V_1) shows that these same areas are also poorly ventilated, indicating the presence of obstructive lung disease. This impairment in ventilation is also very well demonstrated in the washout portion of the 133-Xenon study which shows multiple foci of residual radioactive Xenon resulting from poor ventilation in these areas. The data from the study on this patient were processed by a computer and some of the analyses are shown in Figure 2. The computer output provides quantitative determinations of regional ventilation-perfusion (V/Q) ratios and 133-Xenon clearance times (T½ seconds). The normal (V/Q) ratio is about one.[2] In this study considerable variation in the (V/Q) ratio is demonstrated, particularly in regions also showing prolonged clearance half-times. These data indicate the severity of impairment of pulmonary function in patients with lung disease (Figures 3, 4, 5, 6).

Renal Function

For this examination 131-Iodohippurate (200 uCi) was administered intravenously to evaluate the renal function[8] in a patient with severe scoliosis. Selected scintiphotograms are shown in Figure 3.

At three minutes after intravenous injection, an accumulation of radioactivity is seen in both kidneys. Later scintiphotos show gradual excretion from the kidneys into the bladder. The data from this study were processed by a computer to provide quantitative information relating to the flow of radioactive material through the kidneys and into the bladder. The rapid accumulation and prompt excretion by both kidneys in this examination is an example of normal renal function despite severe scoliosis.

Cardiac Angiography:

A radionuclide angiogram[9,10] is shown in Figure 4. For this examination, a dose of 15 millicuries of 99mTc-pertechnetate was injected intravenously as a bolus. Serial scintiphotograms of the anterior projection of the heart taken at two-second intervals show the flow of the radioactive material through the heart and lungs. In this study, an abnormal concentration of radioactivity

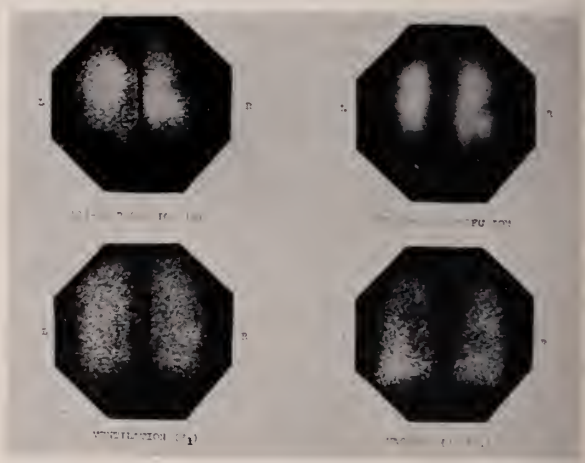


Fig. 1—Selected lung scintiphotos showing: (a) 133-xenon perfusion; (b) 99mTc macroaggregated perfusion; (c) 133-xenon ventilation; (d) 133-xenon washout.

TABLE 1

Nuclear Medicine

A. LABORATORY

1. Plasma volume
2. Red cell mass
3. Red cell survival
4. Fat absorption
5. Vitamin B_{12} absorption
6. Ferrokinetics
7. Immunoassay procedures
8. Radiopharmaceutical preparation
9. Thyroid hormone
10. Exudative enteropathy

B. ORGAN FUNCTION

1. Thyroid
2. Kidneys
3. Liver
4. Lungs
5. Pancreas
6. Bones
7. Heart
8. Spleen
9. Cerebrospinal fluid

C. ORGAN VISUALIZATION

1. Brain
2. Thyroid
3. Lungs
4. Heart
5. Stomach
6. Liver
7. Spleen
8. Kidneys
9. Bones
10. Pancreas
11. Subarachnoid space
12. Placenta
13. Parathyroid

D. REGIONAL BLOOD FLOW

1. Brain
2. Heart
3. Great vessels
4. Lungs
5. Extremities
6. Liver

E. THERAPY

1. Hyperthyroidism
2. Thyroid carcinoma
3. Polycythemia vera
4. Leukemia
5. Effusions
6. Subarachnoid tumors
7. Bone metastases

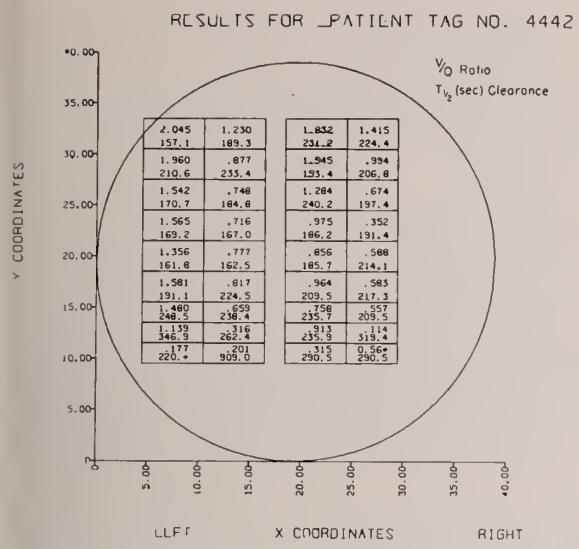


Fig. 2—Computed output showing regional lung V/Q ratios and 133-xenon clearance times.

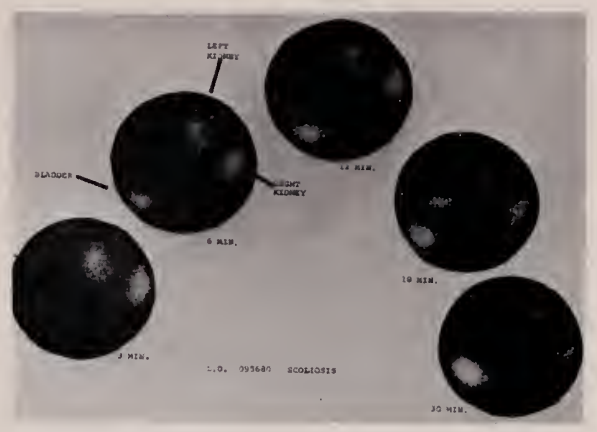


Fig. 3—Selected scintiphotograms showing the flow of 131-Iodohippurate through the kidneys and into the bladder.



Fig. 4—Scintiphotograms taken at two-second intervals showing the flow of 99mTc pertechnetate through the heart and demonstrating a left ventricular aneurysm.



Fig. 5—Right lateral scintiphotogram obtained at 30 seconds postinjection showing an abnormal accumulation of radioactivity in the posterior temporal parietal area. (Reproduced courtesy of Amer J. Roentgenology 109:4 707-713, 1970).



Fig. 6—Repeat Tc^{99m} brain study following surgery indicates no abnormal findings, scintiphotogram taken at 20 seconds postinjection.

in the region of the left ventricle represents an aneurysm.

Cerebral Arteriovenous Malformation

This 18-year-old male was referred for further evaluation of a right cerebral arteriovenous malformation which had been partially resected.[11] Neurologic examination indicated a mild left hemiparesis and a left homonomous hemianopsia. A lateral scintiphotogram obtained at 30 seconds after an intravenous injection of 10 millicuries of Tc^{99m} demonstrated a large abnormal focus of activity in the right posterior temporal parietal area extending posteriorly and superiorly toward the superior sagittal sinus (Figure 5). This defect persisted in a later scintiphotogram taken at 45 minutes post injection. Subsequent to this study a right brachial angiogram confirmed the presence of an AV malformation supplied by an enlarged right posterior cerebral artery and draining via numerous large cortical veins into the superior sagittal sinus. Surgery was performed to remove the AV malformation.

A postoperative rapid flow and static scintiphotographic study was within normal limits (Figure 6). Graphs of radioactivity passing through the region of the malformaiton were obtained via computer analysis of the preoperative and postoperative scintiphotographic studies. The postoperative scintiphotographic study indicates a normal pattern of flow in both the areas of the previous arteriovenous malformation and sagittal sinus. The patient experienced significant clinical improvement after surgery.

Case 2

Jaundice

A 50-year-old white female was admitted for evaluation of prolonged jaundice, with a tender liver and recurrent febrile episodes. Routing X-ray studies were negative. Liver scintiphotograms using 2 millicuries of Tc^{99m} sulfurcolloid demonstrated a large (filling) defect in the posterior superior aspect of the right lobe thought to be compatible with an abscess (Figure 7). At surgery



Fig. 7—Four views of a liver study using 2 mCi Tc^{99m} sulfurcolloid. Note the large defect in the superior portion of the right lobe.

75 ml of pus were drained from an encapsulated abscess, after which the patient made an uneventful recovery.

Comments and Conclusions

The future of Nuclear Medicine shows much promise. Continued advancements in the quality of radiopharmaceuticals and instrumentation including computer processing of data will increase the diagnostic information obtained from Nuclear Medicine studies. It should be emphasized that computer processing of data should not be considered a limiting factor to the practice of Nuclear Medicine. Although several of the case studies presented in this article involve the use of a computer, the appropriate clinical interpretations could have been made adequately utilizing the scintiphotographic images alone.

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Delayed Anemia

In Erythroblastosis Fetalis

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In recent years the literature on hemolytic disease of the newborn has emphasized amniotic fliud examination, intrauterine transfusion, phototherapy and prophylaxis with Rh Immune Globulin. These advances in the diagnosis, treatment, and prevention of erythroblastosis fetalis have diverted attention from, but not altered the importance of prenatal blood typing, antibody screening and post delivery hemoglobin determinations as indicators of possible hemolysis.

We present here nine cases of erythroblastosis fetalis. The first four (Table 1) had appropriate prenatal studies which led to early diagnosis. These cases are of interest because the expected hemolysis and postnatal anemia were delayed in onset. They illustrate the importance of careful postnatal followup in infants only mildly or moderately affected. In the second group of five cases (Table 2) correct diagnosis was delayed because of omission or errors in blood typing and antibody screening or failure to study the infant.

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See editorial, page 457.

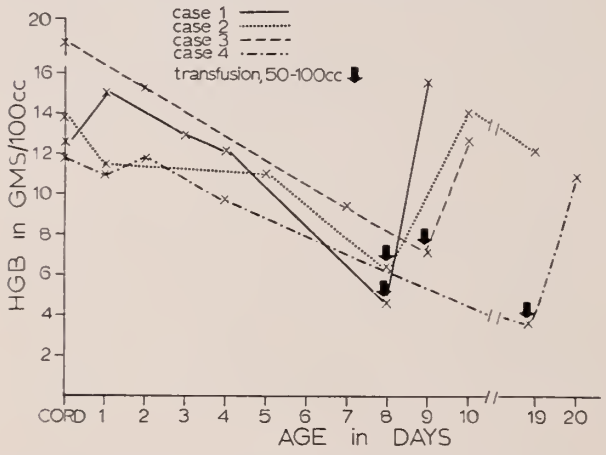
Discussion

Severe erythroblastosis fetalis is characterized by development of anemia due to autohemolysis of erythrocytes coated with maternal antibodies. Prenatal studies including antibody titers and amniocentesis were used to predict the condition of the fetus and its need for therapy in Cases 1-4 (Table 1). Three of the four women (Cases 1, 2, 4) had previously delivered affected infants. However, at birth the infants of the present pregnancy did not show evidence of severe hemolytic disease. Anemia requiring transfusion did not develop until eight and nine days (Figure). The need for transfusion in Cases 1-3 was determined by development of pallor, lethargy, failure to nurse and frequent measurement of their hemoglobins. The two-week interval between discharge

TABLE 1
Cases with Appropriate Prenatal Testing in which Onset of Anemia was Delayed

Case	Age	Gravidity	Past history	Antiglobulin Antibody titer (Rh_o(D)	Amniocentesis	Comment
1	28	3	One erythroblastotic infant	256	23 & 28 weeks Lower Zone II 33 weeks Zone I	Hemoglobin of infant dropped 8 grams in 4 days
2	43	8	Two previously affected infants	128	26 & 28 weeks Zone II 35 weeks Zone I	Mildly affected premature infant with gradual drop in hemoglobin
3	30	3		1	20, 22 & 30 weeks Zone I	Titers not followed
4	38	6	Two previously affected infants	512	35 weeks Zone I	Hemoglobin of infant not closely followed

and followup hemoglobin in Case 4 is too long. Though this patient had good prenatal care she could be added to the second group of cases where errors in management affected the diagnosis. Delayed anemia may also occur in infants that have been treated for erythroblastosis by exchange or simple transfusion. All moderately or severely affected infants should be followed with weekly hemoglobins until they are stable. Parents should be instructed to report to the physician if difficulty in nursing or lethargy develops.



Figure—Serial hemoglobin values in four infants with delayed onset of anemia. Note prompt response to transfusion of 50-100 cc of packed red cells.

Authors disagree as to the cause of delayed onset of anemia in erythroblastosis fetalis. Some have published case reports showing evidence of bone marrow hypoplasia.[1,2] However, Dillon and Krivit,[3] in a study of serial bone marrow specimens from fourteen affected infants, could find no convincing cases of hypoplasia and, on the contrary, noted that marrows showed erythroid hyperplasia proportional to the severity of anemia. Support for their observations was obtained in Case 7 where marked normoblastic hyperplasia in the marrow and extramedullary hematopoiesis were present at autopsy of an eleven day old infant that died shortly after transfusion.

Importance of Prenatal Testing

The second group of cases (Table 2) re-emphasizes the need for all pregnant women, whether Rh positive or Rh negative, to have ABO and Rh typing, and screening for irregular antibodies in each pregnancy. Recognition of the etiology of the anemia in the infants in Cases 5-9 was delayed because of errors of omission and commission. The most common error was failure to do maternal antibody screening and identification (Cases 5-9) which was compounded by mistyping of the mother's blood as Rh positive (Cases 5-8). Had antibody screening been done in these pa-

TABLE 2
Cases in which Diagnosis was Delayed because of Omission or Technically Incorrect Performance of Routine Tests.

Case #	Mother: Past History	Mother: 1/antibody titler (Rh_o)	Infant: Lowest Hgb gm/100 cc	Infant: Age (days) transfused	Comment
5	4 unaffected pregnancies	64	11.9	4	Mistyped as RH positive No prenatal antibody screening
6	Transfusion of Rh positive blood	1024	5.5	12	Mother typed Rh positive in previous pregnancy. No typing or antibody screening during pregnancy
7	2 unaffected pregnancies	1024	2.4	11	Typed as Rh positive in previous pregnancy. No studies this pregnancy.
8	7 unaffected pregnancies	64	7.4	30	Incorrectly typed. No prenatal antibody screening.
9	Transfusions	32*	3.6	16	No cord blood testing or hemoglobins on infant from Rh positive mother known to have atypical antibodies

*Anti-rh "(E).

tients[5-8] it would have raised a question about the results of typing since anti-Rh_o(D) does not usually occur in Rh_o(D) positive individuals. Errors in blood typing, particularly when done by untrained personnel occur with some frequency. In a large metropolitan hospital 3.2 percent of 280 obstetrical admissions who had been previously typed in the doctor's office were found to be in error.[4] In a California study,[5] laboratory factors were contributory in 35 percent of 328 deaths due to erythroblastosis.

The importance of testing in each pregnancy is illustrated by Cases 5 and 8 where three and six apparently normal pregnancies preceded the child with erythroblastosis.

Case 9 points out the importance of typing and antibody screening in routine prenatal studies on Rh positive women. This gravida 3 para 2 Caucasian had a placenta previa and required Caesarean section. Though it was known that she was sensitized to Kell, Fy(a) and rh"(E) no studies were obtained on the infant who at sixteen days of age was admitted to another hospital with "unexplained" anemia. In a study of over 27,000 Rh positive pregnant women, 1.3 percent had atypical antibodies.[6] In addition to delivering unexpected erythroblastotic infants, these sensitized women can present as transfusion problems that may be difficult to solve in an emergent situation.

Acknowledgment

The assistance of Drs. Charles Chedister, Norman Horns, Edward Segal and the several physicians who treated the mothers and infants is gratefully acknowledged.

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Medullary Syndrome

This syndrome comprises one of the clinical variations produced by thrombosis of the anterior spinal artery that supplies the medulla oblongata. The thrombosis occurs near the site where the vessel has its origin from the vertebral artery. Spiller in 1908 first postulated a syndrome that might result from occlusion of the uppermost portion of the anterior spinal artery. It occurs rarely; Davison reported a total of four cases in 700 cerebrovascular accidents that came to autopsy.

The clinical features consist of contralateral pyramidal tract signs of the trunk and upper and lower extremities, contralateral loss of discriminative sensibility in the arms and legs, and occasionally ipsilateral paralysis and atrophy of the tongue. The syndrome may be unilateral or bilateral. If bilateral it is characterized by a spastic tetraplegia with loss of sensation below the lesion. Sphincter and bladder incontinence are usually present. In anomalies where only one anterior spinal artery exists, both pyramids and medial lemnisci may be involved.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

High Velocity Missiles

The Importance in Arterial Wounds and Fractures

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THE AMPUTATION rate is significantly higher in arterial wounds associated with fracture compared with arterial wounds without fracture.[1] However, the reason for the increased amputation rate has not been properly defined. The present report on Viet Nam casualties confirms previous observations and shows that the increased amputation rate in cases with associated fracture is a direct consequence of wounding by high velocity weapons rather than due merely to the presence of the associated fracture alone.

Study Group

The 248 patients in the study group had sustained arterial injuries from hostile fire and had received initial wound care in Viet Nam. All were admitted to the USAF Hospital, Clark AFB, Philippines, between 1 July 1965 and 31 December 1966. Of the 269 arterial injuries of the extremities, 171 (63.6%) involved major arteries and 98 (36.4%) involved named minor vessels. Fifty-eight of the 171 major arterial injuries and 71 of the minor injuries had associated fractures (Table 1). The distribution of wounding and incidence of associated fracture for the entire series is given in Table 2.

As expected, the incidence of associated fracture was greater the more distal the site of injury. Twenty-seven percent of these patients also had associated thoracic and/or abdominal wounds.

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TABLE 1
Incidence of Associated Fracture in Major and Minor Arterial Injuries of the Extremity

Category of Injury	No. of Injuries	No. of Fractures	% Fractures
Major	171	58	(33.9)
Minor	98	71	(72.4)
Total	269	129	(47.9)

Wounding Agent

The cause of missile injury in Viet Nam has changed significantly compared to World War II and the Korean War.[2] In the latter conflicts, at least 75 percent of the battle casualties resulted from fragmentation injury and only 25 percent from gunshot wounds. However, in Viet Nam approximately 50 percent of all wounds resulted from high velocity small arms fire.[3] This difference is probably due to the increased number of search and destroy missions in which the individ-

TABLE 2
Arterial Injuries of the Upper and Lower Extremities and Incidence of Associated Fracture

Artery	No. of Injuries	No. of Fractures	(%) Fractures
Upper extremity			
Axillary	9	2	(22.2)
Brachial	38	22	(57.8)
Radial	14	11	(78.5)
Ulnar	14	10	(71.4)
Total	75	45	(60.0)
Lower extremity			
Common Femoral	10	1	(10.0)
Superficial Femoral	51	14	(27.4)
Deep Femoral	3	0	(0.0)
Popliteal	63	19	(30.1)
Anterior Tibial	26	21	(80.7)
Posterior Tibial	35	22	(62.8)
Peroneal	66	6	(9.1)
Total	194	83	(42.7)

ual is more exposed to sniper fire.

The importance of the high velocity agent as a cause of associated fracture in shown in Table 3. The overall incidence of associated fracture in major artery injury was nearly twice when the wounding agent was a bullet compared with a fragment ($p < 0.001$) (Table 3). However, when the data were regrouped with respect to the extremity involved, certain notable differences were found (Table 4). In the case of the upper extremity, wounds with associated fracture were significantly more often produced by bullets than by fragments ($p < 0.01$). However, in the lower extremity, the difference in incidence between bullet and fragment as the wounding agent was not significant whether a fracture was caused or not. This difference between the extremities is explained by the fact that approximately 50 percent of the fragmentation injuries of the lower extremity resulted from stepping directly onto land mines. In such cases, this proximity to the wounding agent caused a blast effect, or allowed several discharged fragments to strike with high initial velocities and produce wounds similar in effect to those caused by high velocity bullets.

Treatment

Ligation

In minor arterial injuries, the vessel was ligated 83.7 percent of the time, whether a fracture was present or not.

Anastomosis—Repair

Of the 16 minor vessels not ligated, 11 were of the tibial-peroneal group with seven associated fractures, and five were of the radial-ulnar group with four associated fractures. For these 16 vessels, a direct anastomosis was carried out nine times and a lateral repair seven times, but there was no correlation between the type of treatment and the presence of a fracture.

As far as the *major arterial injuries* are concerned, an associated fracture had no influence on the initial type of treatment. Vein graft, vein patch, anastomosis, lateral repair, prosthesis and ligation were used with about the same frequency in major arterial injuries with fracture as in those without fracture. Moreover, where the initial treatment was some form of repair (initial ligations excluded, the type of treatment selected was not influenced by the type of wounding agent, whether a fracture was present or not (Table 5).

Immobilization

All fractures associated with minor arterial injuries were immobilized by plaster casts or splints except for one case of combined anterior and posterior tibial artery injury in which the tibia was immobilized with an intramedullary rod. For fractures associated with major arterial injuries, 74.1 percent were immobilized in plaster, whereas 25.9 percent were treated with internal fixation. The incidence of internal fixation per major vessel is shown in Table 6 along with the types of internal fixation used. Internal fixation was used in these patients because at the time of arterial repair the unstable fracture was seen to angulate sufficiently to compromise arterial flow. One of these patients who had a superficial femoral artery injury underwent internal fixation at Clark Air Base at the time

TABLE 3
Wounding Agent in Major Arterial Injuries of the Extremity With and Without a Fracture

Category of Injury	No. of Injuries	% By Wounding Agent Bullet	Fragment	Closed
Major				
Fracture	58	60	35	5
No Fracture	113	28	71	1

TABLE 4
Wounding Agent in Arterial Injuries of the Upper and Lower Extremity With and Without a Fracture

Category of Injury	No. of Injuries	% By Wounding Agent Bullet	Fragment	Closed
Upper Extremity				
Fracture	45	64	36	—
No Fracture	30	30	70	—
Lower Extremity				
Fracture	84	37	59	4
No Fracture	110	26	73	1

TABLE 5
Wounding Agent and Type of Repair in Major Arterial Injuries With and Without a Fracture

Repair	No of Injuries	% By Wounding Agent Bullet	Fragment	Closed
Associated Fracture				
Vein Grafting	26	61	35	4
Direct Suture (2 Prostheses)	28	61	32	7
No Fracture				
Vein Grafting	57	24	74	2
Direct Suture (1 Prosthesis)	46	33	67	0

TABLE 6
Types of Internal Fixation Used in Fractures Associated With Major Arterial Injuries

Artery	Fractures	Internal Fixation
Brachial	22	5
Superficial Femoral	14	7
Popliteal	19	3
Total	55	15*

*Includes 10 intramedullary rods, 3 plates, 1 screw and 1 pin.

of re-operation for thrombosis of a vein graft because angulation and occlusion occurred after replacement of the graft.

Amputation

Amputation may be taken as the endpoint of failure in the treatment of arterial injuries of the extremity. Ischemic gangrene is the leading cause of amputation after arterial repair is attempted. However, to a lesser degree limbs may be sacrificed because of gas gangrene, unrelenting infection accompanying extensive associated soft tissue or osseous injury, and because of sequelae of major peripheral nerve injury.

Results

As a consequence of the 269 major and minor arterial injuries of the extremity in this series, there were 73 amputations (27.7%). Seventy amputations (95.9%) resulted from ischemic gangrene, and three from gas gangrene. In the latter three patients, gas gangrene developed after successful repairs of superficial femoral and popliteal artery injuries (neither associated with a fracture), and in one patient after ligation of anterior and posterior tibial artery injuries with an associated fracture.

When initial ligations and gas gangrene were excluded from consideration, the amputation rate for major arterial injuries of the extremity with fracture was twice as high as when there was no associated fracture ($p < 0.01$) (Table 7). With the minor arterial injury group, however, the difference in amputation between those patients with a fracture and those without proved not to be significant as might be assumed at first glance ($p < 0.30$). The lack of significance between these two latter groups probably relates to the fact that the vast majority (83.7%) of all named minor arterial injuries were treated by ligation and that in the majority of injured limbs two or three of the minor vessels were ligated.

The findings of DeBakey and Simeone in an analysis of World War II casualties were similar to those in the present series (Table 8). The relative increase in the amputation rate in both series for major arterial injuries with an associated fracture does not seem to be a reflection of the type of initial treatment. The 154 major arterial injuries of the present series were repaired initially, while the 277 injuries analyzed in the World War II series were selected for study from 1,774 arterial wounds, 92.4 percent of which were ligated initially.

No significant difference in the amputation rate was found when internal fixation was compared with external immobilization. However, because of the small number of cases of internal fixation in this series, no significant recommendations can be made for its use. Internal fixation may certainly be of benefit in selected cases when stability and angulation of the fracture threaten to compromise the vascular repair.

An important factor to be considered in the influence of associated fracture on the amputation

TABLE 7
Influence of Associated Fracture Upon the Amputation Rate in Major and Minor Arterial Wounds of the Extrimty

Category of Injury	No. of Injuries	Number of Amputations	% Amputation
Major			
Fracture	53	26	49
No Fracture	101*	26*	26
Minor			
Fracture	70†	11†-	16
No Fracture	27	1	4

*Excluding 2 cases with gas gangrene.
†Excluding 1 case with gas gangrene.

TABLE 8

Series	Fracture		No Fracture	
	No. of Injuries	% Amputed	No. of Injuries	% Amputed
DeBakey & Simeone[1]				
World War II	111	61	166	43
Present Series				
Viet Nam	53	49	101	26

rate was the type of wounding agent involved. In a group of 26 amputations from major arterial injuries of the extremity with fracture, the most frequently responsible wounding agent was a high velocity bullet (50%), whereas in a corresponding group without fracture it was a fragment (77%) ($p < 0.05$) (Table 9).

TABLE 9

Fracture	Number of Amputations*	Wounding Agent, % Bullet	Fragment	Closed
Yes	26	50	39	12
No	26	23	77	0

*Excluding amputations due to gas gangrene and where the initial treatment of the arterial injury was a ligation.

Conclusions

When vascular injuries of the extremity are associated with fractures, the amputation rate can be expected to be significantly higher than in the absence of fractures. However, the significant correlation is not between the presence of a fracture, *per se,* and amputation, but rather between amputation and a high velocity wounding agent. Fracture is merely a consequence of the high velocity wound in addition to more soft tissue damage and disruption of the collateral circulation; collectively, these increase the chance for ischemic gangrene and the need for amputation.

The type of treatment used to manage major arterial injuries does not seem to have any influence on the relative outcome in wounds associated with fracture compared to those without fracture. The amputation rate is significantly higher with associated fracture than without in both this series in which 90 percent of major arterial injuries were treated initially by some type of vascular repair and the World War II series of DeBakey and Simeone[1] in which 92 percent were treated initially by ligation. However, the net results with and without fracture are relatively better in Viet Nam than in World War II because of the current use of arterial repair rather than ligation.

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Cover Photo

"Flower Festival"

The 35 mm slide of the cover photo was taken by Dr. Murray S. Locke while vacationing in the Netherlands. Pictured is the hardy, Spring-blooming bulb, *Amaryllis hippeastrum,* one of many varieties seen at the flower festival in Alkmaar.

Dr. Locke is a psychiatrist in private practice at the Minneapolis Clinic of Psychiatry and Neurology, and on the staff of Fairview Southdale, Methodist, and Glenwood Hills Hospitals. He is a Clinical Assistant Professor in the Department of Psychiatry at the University of Minnesota.

O lead me, queen sublime, to solemn glooms
Congenial with my soul; to cheerless shades,
To ruin's seats, to twilight cells and bow'rs,
Where thoughtful Melancholy loves to muse,
*Her fav'rite midnight haunts.**

*Thomas Warton, "The Pleasures of Melancholy"

Concomitant Myelomonocytic Leukemia and Multiple Myeloma

LUIGI TADDEINI, M.D., F.A.C.P.* and WAYNE SCHRADER, M.D.*

A NEW SYNDROME of plasma cell dyscrasia culminating in acute leukemia has been recently recognized.[1,2,3,4,5,6,7] In all reported cases of this syndrome, the appearance of myelomatosis preceded the development of acute leukemia, and in all instances the patients had received treatment with cytotoxic agents prior to the terminal leukemic crisis, suggesting the possibility that prolonged chemotherapeutic suppression of multiple myeloma may act as a leukemogenic factor.

We have observed a patient in whom acute myelomonocytic leukemia and multiple myeloma were simultaneously present at the time of diagnosis. The association of these two conditions, in a patient who had neither received prior therapy, with alkylating agents nor radiation treatment has not to our knowledge, been previously reported. The description, course, and postmortem findings of this unique case forms the subject of this paper.

Case Report

A 73-year-old caucasian male was referred to St. Paul-Ramsey Hospital in December 1968, because of anemia and hepatosplenomegaly. He had received six units of blood prior to admission. The patient bruised easily and had leg pain for 10-12 months. There was no history of chronic infection, toxic or radiation exposure. Physical examination revealed large ecchymotic areas on both arms, and generalized petechiae over the anterior surfaces of the lower extremities. The liver was felt three cms below the right costal margin, and the spleen was palpable 6 cms below the left costal margin. Several lymph nodes 2-3 cms in diameter were palpable in the left axilla, and in both inguinal regions.

The hemoglobin was 10.8 gms%, and the white count was 9,000 with 38% PMNS, 24% lymphocytes, 11% monocytoid cells, 3% basophils, 8% myelocytes, 1% plasma cells, and 15% blasts. There were 5 normoblasts/100 WBC. Platelet count was 16,000 and the reticulocyte count was 2.8%. The creatinine was 1.3 mg and BUN 38. Bone marrow examination revealed a hypercellular specimen with 50% blasts (Figure 1). There was a decrease in number of megakaryocytes as well as 8.8% mature and immature plasma cells. The blast cells, particularly in the peripheral blood, had a monocytoid appearance. They stained Sudan black positive and an occasional Auer rod could be found. Erythropoiesis was decreased with megaloblastoid features.

Because of the increased number of plasma cells in the marrow, a serum electrophoresis was obtained. This revealed a monoclonal peak of 1.7 gm% in the gamma region. Bence-Jones protein was negative in the urine and bone survey demonstrated areas of increased radiodensity in the medullary canal of the right tibia.

The patient was treated with a combination of 6 mercaptopurine, prednisone, vincristine and methotrexate as well as platelet and blood transfusions. A serum electrophoresis repeated two weeks after initiation of treatment revealed an even greater sharp spike of 2.9 gm % in the gamma region (Figure 2) and immunoelectrophoresis characterized the spike as an IgG immunoglobulin lambda chain type.

Bone marrow aspiration repeated after eight weeks of chemotherapy revealed a hypercellular marrow with 4.3% blasts, and 15% abnormal plasma cells (Figure 3). Marrow biopsy showed an overwhelming predominence of atypical plasma cells diffusely distributed throughout

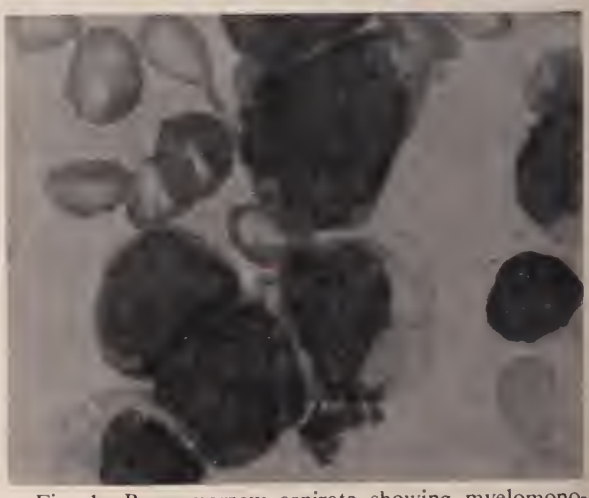


Fig. 1—Bone marrow aspirate showing myelomonoblasts at the time of initial diagnosis. (Wright's stain—Original magnification x 1000).

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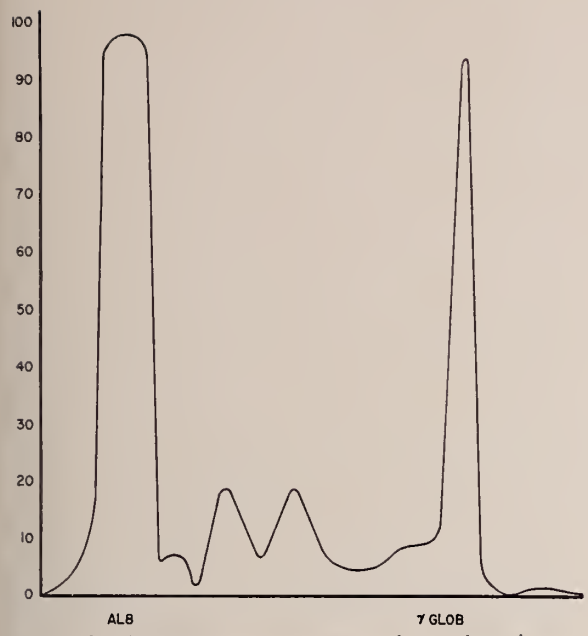


Fig. 2—Cellulose acetate serum electrophoresis two weeks after admission.



Fig. 3—Bone marrow aspirate showing myeloma cells. (Wright's stain—original magnification x 1000).

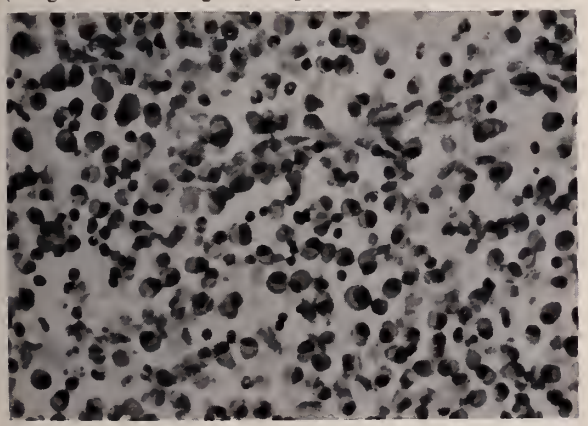


Fig. 4—Bone marrow biopsy demonstrating diffuse infiltration with atypical plasma cells (Hemotoxylin and eosin—original magnification x 450).

the bone marrow tissue stroma (Figure 4). Bence-Jones protein was positive in the urine at this time, and the diagnosis of multiple myeloma as well as acute myelomonocytic leukemia in partial remission was made.

The patient was started on small doses of cyclophosphamide but remained severely thrombocytopenic and anemic, requiring frequent transfusions. He died six weeks later of a cerebral hemorrhage.

Postmortem examination revealed an enlarged liver and a moderately enlarged spleen (250 gms) with evidence of extramedullary erythropoiesis. The marrow was hypercellular and was almost entirely replaced by myeloma cells with marked reduction in number of myeloid and erythroid elements. No evidence of a malignant myeloid process could be found.

Discussion

Osserman et al.[1,8] described a patient with a history of chronic urinary tract infection for many years who developed multiple myeloma at the age of 41. He was treated with radiation, urethane and melphalan, and died four years later shortly after developing evidence of acute myelomonocytic leukemia.

Nordenson[9] describe two cases of acute myeloblastic leukemia, and five cases of acute lymphoblastic leukemia, in a review of 310 cases of myelomatosis, but no details concerning the leukemias were given. Edwards and Zawadzki[2] reported the case of a patient who died of acute leukemia ten years after the diagnosis of myelomatosis for which he had received treatment with radiation, urethane and cyclophosphamide.

More recently Kyle et al.[3] discussed in detail the occurrence of rapidly progressive acute myelomonocytic leukemia in three patients with myeloma, and in one with primary amyloidosis who had received prolonged courses of melphalan therapy ranging from 30 to 57 months. Because of the remote likelihood of chance association of these two rare hematological disorders, the authors emphasized the possible role of melphalan therapy in the development of acute leukemias in their patients.

Four additional patients with myelomatosis in whom acute stem-cell leukemia developed were described by Andersen and Videbaeck in Copenhagen.[4] Like Kyle's cases all four patients had been given chemotherapy treatment with melphalan for long periods; two of them had had cyclophosphamide as well, and two had had radiotherapy. The Copenhagen workers reasonably pointed out that the long continued use of an alkylating agent might be capable of evoking

acute leukemia in man. They also postulated, however, that the terminal acute leukemia might be the result of a natural evolution of multiple myeloma and that a close relationship might exist between myeloma cells and blast forms.

Holland, in an editorial review of this subject[6] stated that in the past three and one half years, he and his colleagues have observed five cases of myelomatosis culminating in acute leukemia after prolonged chemotherapy.

Farhangi and Osserman[5] have lately observed two more cases of acute myelomonocytic leukemia as a late complication in plasma cell dyscrasia. The authors postulated that the development of leukemia in multiple myeloma is possibly related to a relationship between monocyte and plasma cells, the former representing a more primitive defense mechanism than the plasma cell-immunoglobulin system in the course of phylogenetic evolution.

Paraproteins have been reported in acute leukemia without myeloma.[10,11,12,13] Recently Thijs et al.[14] described a case of blast cell leukemia with IgA paraproteinemia and Bence-Jones protein Kappa type. Immunofluorescence investigations provided evidence that some blast cells contained K type light chains indicating that at least part of the blast cells could be considered immunologically active.

In our patient the appearance of acute leukemia could not be attributed to previous chemotherapy or radiation exposure. Even such rare conditions as myelomatosis and acute leukemia may be fortuitous, but on the basis of previous reports suggesting a relationship between blast cells, and myeloma cells this seems an unlikely possibility. The simultaneous presence of blast cells and myeloma cells in the same individual supports, in our opinion, the view of the existence of an evolutionary connection between these two types of cells, but unfortunately no immunofluorescence studies[14] were done to verify this relationship.

It is of interest that intensive chemotherapy produce in our patient remission of acute leukemia but an apparent increase of myeloma cells in the marrow and an increase of paraproteins in the serum suggest the possibility of a nearly complete transformation of one type of malignant proliferation into the other. The postmortem findings confirmed the presence of an overwhelming proliferation of myeloma cells but no evidence of acute leukemia.

As pointed out in an editorial review of this subject[7] the possible relationships of acute leukemia, myelomatosis and various chemotherapeutic agents can only be confirmed by careful, continuous reporting until adequate statistics are obtained. The case reported in this paper indicates, that the two hematological conditions can occur independently from the effect of cytotoxic drugs, and perhaps suggests that they may be part of the spectrum of the same disease.

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Case Report

Traumatic Luxation of the Testis

JOSEPH N. AQUILINA, M.D.*

THE NORMALLY descended testis can be dislocated along fascial planes or through normal anatomic apertures by sheer traumatic force. Ockuly in 1946, while describing a case of bilaterally luxated testis, established the principle that only a previously normally descended testis can be classified as a traumatically luxated one.[16] The testis itself is usually unharmed but it may be separated from its epididymis through a partial tear or may perhaps have torn fascial coverings.[13]

Historical Review

The first cases of testicular dislocation were published by Claubry in 1818 in Paris, and later by Liddon in London in 1858.[4-11] In 1890, Howlet published a case of a normally descended testis dislocated into the fascial coverings of the penis.[8] About 50 cases have so far been published in the literature and only 10 of these have been bilateral.[14-16] Guiteras published a case in which the testis was found on the side of the penile shaft; and Kaursch, another in which the testis was luxated to the undersurface of the penis.[6-10] The cases reported by Howlet and Guiteras had both been reported to have suffered tearing of the epididymis from the testis during the accident.[6-8] Schuerer-Waldheim excised an internally dislocated testis after two years because it had developed a seminoma.[17] Jurinka and Bancale each reported a case of traumatic luxation of a testis into the acetabulum.[2-9] Sethi et al. reported on a testis dislocated beneath the prepuce for a period of two years, during which time the patient had married and sired a daughter.[18] Only two cases of testis luxation into the abdominal cavity have been reported.[17-18]

Clinical Features

These injuries usually occur as a result of a wheel passing over the genital region or from a straddle injury. The most common associated injuries are pelvic fractures, femoral fractures, dislocation of the hip, contusion of the inguinal ligament and skin contusion.[13]

The classification of Alyea (1929) is still accepted today.[1] Morgan suggested that this classification should not include those testes which are luxated as a result of a scrotal tear.[13] This classification of testes luxated superficially includes those luxated to the crural, penile, perineal, superficial inguinal and pubic regions; those classified as luxated internally include those in the inguinal or femoral canal, as well as abdominal and acetabular luxations. The most common superficial luxations are found in the superficial inguinal and pubic regions.

Case Report

A 47-year-old white male was pulling a car from a snow bank with a wrecker truck. While doing this he noted that the cable did not wind itself properly on the winch. He therefore tried to disentangle this by unwinding the cable and then rewinding it. During the process of winding the cable he accidentally stepped inside a couple of loops of cable and was caught at the upper thighs and left dangling from the winch. Luckily this stalled and shut off the motor. After his rescue by a farmer, the patient was admitted to the hospital. His injuries included a fractured left femur, fractured distal right ulna, partial amputation of the third and fifth fingers, as well as pressure necrosis and skin contusions circumferentially around his thighs. He was also noted to have an abdominal mass about three inches above the right inguinal ligament. When I saw him, the third day after the accident, the scrotum on the right was well developed and empty (positive Brockman sign); that on the left had a normal testis. The right testis was palpable just beneath the subcutaneous tissues where the mass had been described. There was a generalized hematoma of the scrotum. No panile injuries were present. Under gentle massage, the testis was replaced into the scrotum with some discomfort to the patients.

Comments

The first manual reduction of a dislocated testis was performed by Connor in 1861,[5] the first operative reduction by Nicholas in 1899.[15] In 1929 Alyea reviewed 20 cases in the literature and stated that 11 patients underwent open reduction and three closed reduction; six were not treated.[1]

*Mankato Clinic, Mankato, Minnesota. Present location: 3406 Davenport, Saginaw, Michigan.

Herbst and Polkey reviewed 93 reported cases, only 39 of which were regarded as true traumatic dislocated testes; the others were either cases of rupture of the testis, effort luxation or dislocation by a truss of a congenitally ectopic testis.[7]

The same authors performed an experimental study of testicular luxation and concluded that while luxation can occur with relative ease, reduction was often difficult.[7] They also showed that fascial coverings of testes were often damaged during the process of traumatic luxation. This explains at least two causes for difficult testicular reduction: hematoma and edema, and organizing scar tissue. Those who have operated for cryptorchism know that often there are abnormal attachments of Scarpa's fascia to the pubic bone. This was originally described by Browne in 1938.[3] Morgan suggests that when this fold remains after foetal descent of the testis, it may became a factor in preventing reposition.[13] McGregor also described the so-called third inguinal ring which may be a factor in prevention of reduction as well as luxation.[12] It is because of this fascial ring or funnel at the neck of the scrotum that traumatic force has to be of sufficient strength and in the proper direction to force the testis through the ring. In manual reduction of a luxated testis, sufficient pressure has to be exerted to force the testis through this ring. Edema and hematoma may cause a hang-up at this anatomic location. This is where waiting a few days usually pays off. In this case reduction took place without much difficulty on the third day.

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Warnings: Use with discretion during the second and third trimesters of pregnancy and restrict to those pregnant patients not cured by topical measures. Flagyl (metronidazole) is secreted in the breast milk of nursing mothers. It is not known whether this can be injurious to the newborn.

Precautions: Mild leukopenia has been reported during Flagyl use; total and differential leukocyte counts are recommended before and after treatment with the drug, especially if a second course is necessary. Avoid alcoholic beverages during Flagyl therapy because abdominal cramps, vomiting and flushing may occur. Discontinue Flagyl promptly if abnormal neurologic signs occur. Exacerbation of moniliasis may occur. In amebic liver abscess, aspirate pus during metronidazole therapy.

Adverse Reactions: Nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, a metallic, sharp and unpleasant taste, furry or sore tongue, glossitis and stomatitis possibly associated with a sudden overgrowth of *Monilia*, exacerbation of vaginal moniliasis, an occasional reversible moderate leukopenia, dizziness, vertigo, incoordination and ataxia, numbness or paresthesia of an extremity, fleeting joint pains, confusion, irritability, depression, insomnia, mild erythematous eruptions, "weakness," urticaria, flushing, dryness of the mouth, vagina or vulva, pruritus, dysuria, cystitis, a sense of pelvic pressure, dyspareunia, fever, polyuria, incontinence, decrease of libido, nasal congestion, proctitis, pyuria and darkened urine have occurred in patients receiving the drug. Patients receiving Flagyl may experience abdominal distress, nausea, vomiting or headache if alcoholic beverages are consumed. The taste of alcoholic beverages may also be modified. Flattening of the T wave may be seen in EKG tracings.

Dosage and Administration

For Trichomoniasis. In the Female: One 250-mg. tablet orally three times daily for ten days. Courses may be repeated if required in especially stubborn cases; in such patients an interval of four to six weeks between courses and total and differential leukocyte counts before, during, and after treatment are recommended. Vaginal inserts of 500 mg. are available for use, particularly in stubborn cases. *When the vaginal inserts are used,* one 500-mg. insert is placed high in the vaginal vault each day for ten days and the oral dosage is reduced to two 250-mg. tablets daily during the ten-day course of treatment. Do not use the vaginal inserts as the sole form of therapy. *In the Male:* Prescribe Flagyl only when trichomonads are demonstrated in the urogenital tract, one 250-mg. tablet two times daily for ten days. Flagyl should be taken by both partners over the same ten-day period when it is prescribed for the male in conjunction with the treatment of his female partner.

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Children: 35 to 50 mg./kg. of body weight/24 hours, divided into three doses, orally for ten days.

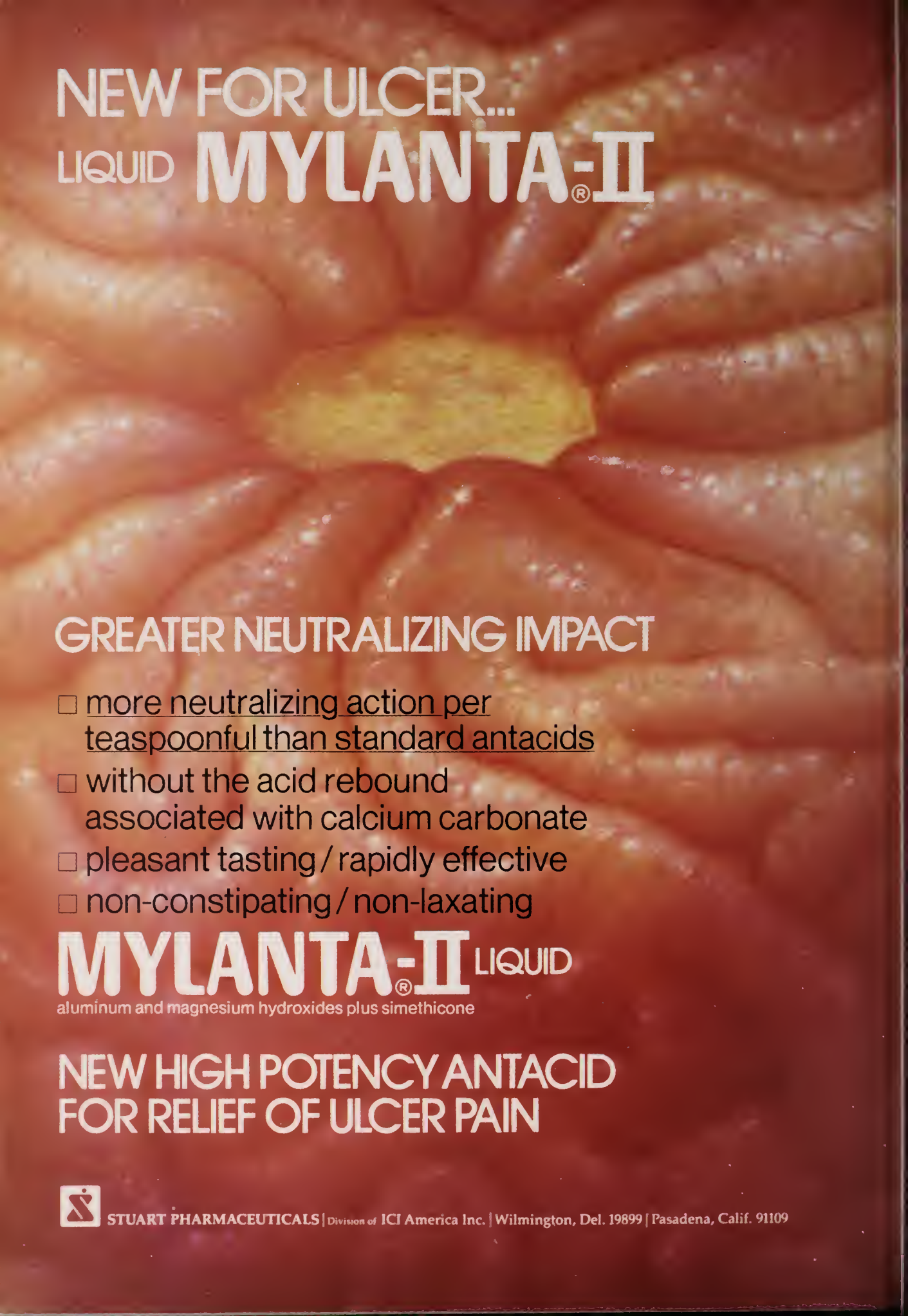
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Editorials

Granulomatous Peritonitis Induced by Cornstarch Powder

THE REPORT by Hornung and Kremen* emphasizes that factors other than bacterial should be considered in the surgical ritual of scrubbing, gowning, and gloving. They advise scrupulous mechanical cleansing of dusting powder from surgical gloves as a part of the preparatory routine. Under certain circumstances absorbable dusting powder U.S.P.[1] (starch-derivative dusting powder), used throughout the world as a dry lubricant for surgical gloves, is implicated in the genesis of a nonspecific foreign body (granulomatous) inflammatory reaction of peritoneal surfaces after operations. A vague but definable clinical syndrome is recognized with an onset two to six weeks after laparotomy. At re-exploration, findings of a sterile peritonitis, ascites, miliary peritoneal nodules, and excessive peritoneal fibrosis are characteristic. Diagnosis is confirmed by microscopic identification of starch material in fluid exudate and within foreign body granulomata.

It is not possible from a single report to define clearly the magnitude of the problem, though the authors suggest that it is probably greater than recognized. During 1971 alone there were at least 15 additional cases reported in the medical literature,[2-7] I am aware of at least one additional documented case referred to the Mayo Clinic in the past year.

The product implicated is prepared by treating cornstarch with epichlorohydrin,[8] a compound described as a skin and kidney irritant and sensitizer.[9] The incorporation of not more than 2% magnesium oxide is said to help keep the starch derivative a fine powder. More recently this dusting powder has been made available in a sterile rapid-drying hand lotion to facilitate lubricating prepared hands just before donning gloves.

Little is known about the derivatives used and little progress has been made in developing safer substitutes; more basic information is needed. Meanwhile surgeons are urged to remember this potential complication, to clean the exterior of surgical gloves carefully with a wet towel, and to repeat cleaning when perforations require reglovving during operations.

W. Spencer Payne, M.D.
Rochester, Minnesota

*See page 427.

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Delayed Anemia

THE POSSIBILITY of unanticipated delayed anemia in hemolytic disease of the newborn is real, serious, and may be fatal. In this issue Strand and Polesky* remind us of two sources of error: failure to test all pregnancies for sensitization, and failure to measure serially hemoglobins of babies with mild hemolytic disease of the newborn. The suggested weekly intervals may not be frequent enough.

When one multiplies the above by the chances of technical laboratory error, secretarial error, garbled phone reports, unidentified loose papers, overloaded mental circuits and the always possible infectious or metabolic causation of neonatal icteric anemia, one is thankful that the authors had only nine cases to report.

In no other common clinical situation is diagnosis and management more dependent upon the accurate processing of laboratory measurements. Only methodical and diligent attention to detail can minimize the possibility of error.

Detlof M. Olson, M.D.
Minneapolis, Minnesota

*See page 439.

An Unusual Complication of Cystourethrography

THE ARTICLE BY Cass and Vitko* in the April issue concerning unusual complications of cystourethrography describes a fairly significant complication of an ordinarily uncomplicated routine procedure done without incident every day in most hospitals. A plain catheter may become impacted, but is a less hazardous instrument than the Foley catheter which can be blown-up intraurethrally or in a ureteral orifice as has been sometimes reported.

The article by Kjelberg referred to in the discussion indicates that the incidence of technical complication is extremely low. This certainly does not mean that the complication rate cannot be reduced by improvement in the technician training programs.

The recommendation that the complication described in the case report could have been averted by introducing the catheter a shorter distance is certainly valid and perhaps this suggestion will be applied by someone reading this article.

Rodger R. Lundblad, M.D.
Minneapolis, Minnesota

See page 335.

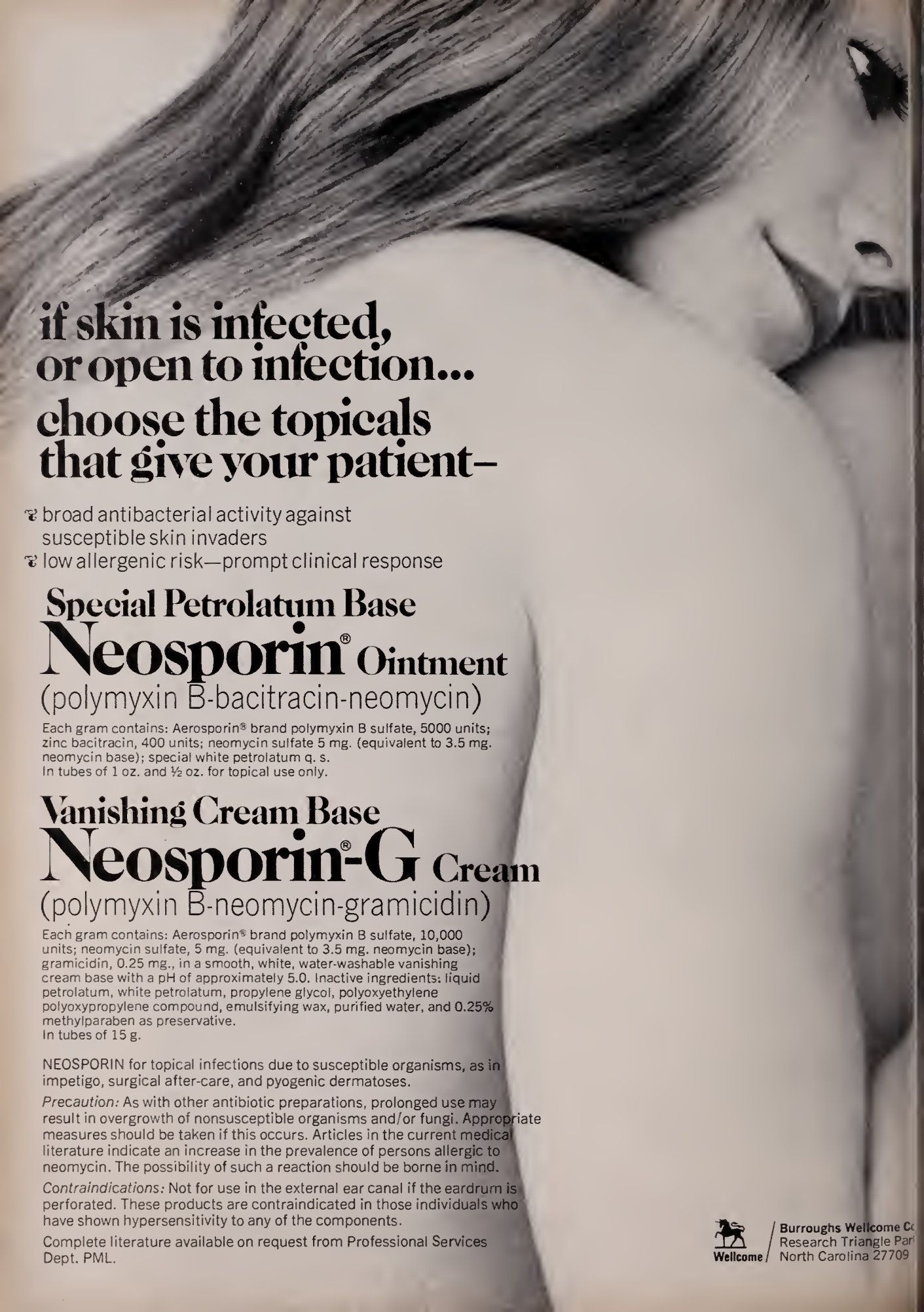
Traumatic Luxation of the Testis

TRAUMATIC DISLOCATION of the testicle, described in this issue by Aquilina, is uncommon, perhaps because the mobility of the organ permits it to bounce away from most vulnerating forces. It is easily recognized if it can be established that the testis was normally placed before the injury. Replacement, either my manipulation or operation, should be simple if the patient's general condition permits. If delay is necessary, or if the abnormality is at first overlooked because of preoccupation with other injuries, fibrosis may prevent successful manipulation, but should not interfere with operation, based upon the principles of orchiopexy. If the epididymis has been avulsed without destroying the testicular blood supply, it should be sutured back in place, although sperm cannot thereafter be transplanted to their normal destination. If the blood supply to the testicle itself has been torn off, the organ had best be removed, since the presence of a small wad of scar tissue will afford the patient but little satisfaction. If the gonad is a solitary one, and the injury is fresh, one should consider cutting it into thin slices and inserting them into slits in a rectus muscle.

After any severe trauma to the testicle, the patient should be warned that atrophy may follow, least he attribute it to the treatment.

C. D. Creevy, M.D.,
Minneaoplis, Minnesota

See page 449.



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The Ruptured Disc Syndrome

To some, bony contriction of the spinal canal implies the syndrome of pseudoclaudication. In his paper published in the April issue, however, Ellison* describes a different syndrome of radiculopathy related to spurs and bony constriction of the entrances to the nerve root canals from the spinal canal. Roentgenograms of oblique views of the cervical spine often demonstrate spurs with clear evidence of narrowing of nerve root canals. Such narrowing in the lumbar area can conceivably be symptomatic, though the larger lumbar intervertebral foramina require hypertrophic changes of greater degree than in the cervical area. Hypertrophy of the ligamentum flavum usually takes place toward the midline in between the vertebral spines and the lamina posterior to the shelf of the ligamentum flavus. Although hypertrophy of the ligamentum flavum can indeed occur laterally, particularly in instances where the disk space is markedly narrowed, such hypertrophy is almost invariably posterior to the shelf of the ligamentum flavum where it cannot involve the nerve root.

While it is possible as indicated by the author's cases for radiculopathy to be produced by the combination of factors he cites, it should be remembered that this certainly is not a common finding, and we must be cautious about recommending surgery on this basis.

Reviewing a great many surgical reports of operations done throughout the country on patients with low back and leg pain who are referred to us with persistence of their symptoms reveals a high percentage of reports describing constriction of the nerve root canal, lumbar spondylosis with hypertrophy of the ligamentum flavum, hypertrophy of facet joints, and slightly bulging disks in combination with hypertrophied ligament. There is perhaps no surgical procedure which gives a better result than that performed for a truly extruded disk fragment. The reverse, however, is unfortunately true. Surgery performed for less clear pathologic changes often leaves scar tissue in and around the nerve roots and patients complaining of continuing pain similar to, or even worse, than they had experienced prior to the exploration.

Thoralf M. Sundt, M.D.†
Rochester, Minnesota

*See page 321.
†Department of Neurosurgery, Mayo Clinic.

Laparoscopic Sterilization*

Recent refinements in lighting, operative techniques, and instrumentation have revived laparoscopy (celioscopy) and it has become an important diagnostic and therapeutic tool in Gynecology. The panoramic view of the pelvis cannot be matched by culdoscopy. Its use in female sterilization has gained popularity because of low morbidity and short hospitalization.* In addition other operative procedures in the pelvis such as biopsy, cautery of small endometriomata, and lysis of adhesions have been described.

Pneumoperitoneum is produced with carbon dioxide or nitrous oxide gas and when general anesthesia is used, Anectine and endotracheal intubation with manual assistance of respiration is advisable. We have laparoscoped a number of patients using intravenous Valium and Nisentil with local abdominal block. This allows dismissal from the anesthesia recovery room after several hours, and assisted respiration is not necessary.

The major demand for laparoscopy at the Mayo Clinic has been for elective female sterilization, even though vasectomy is usually recommended to the couple seeking permanent sterilization.

We continue to remove bilaterally and confirm microscopically a small segment of fallopian tube near the uterine fundus and coagulate the two free ends, left after removal of the tube segment. Postoperative salpingography is not done because of possible tubal distension and production of patency by pressure.

As with most fallopian surgical procedures for sterilization, the possibility of patency re-establishing in the proximal stump of tube exists. However the failure rate must be low provided the round ligament or utero-ovarian ligament have not been mistaken for fallopian tube at the time of laparoscopy.

Laparoscopy is not a simple office procedure

*Larson, Stephen L.: Laparoscopic Sterilization, April issue, page 369, 1972.



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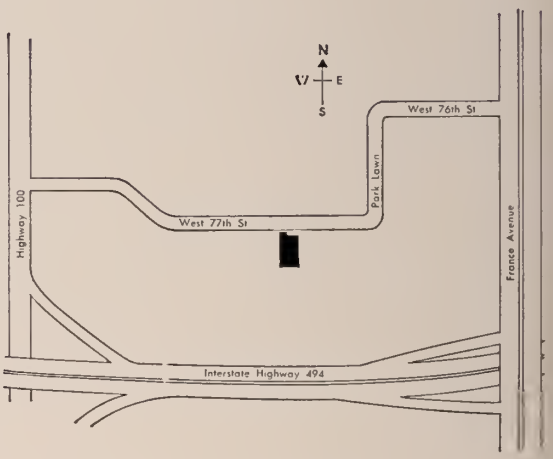
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as intimated by some writers. Complications associated with anesthesia and pneumoperitoneum occur. Bleeding and accidental bowel perforation present potential danger and require immediate laparotomy.

As with all surgical procedures, training and experience lessen the likelihood of complications due to errors in technique and improper patient selection. Laparoscopy will remain an important diagnostic tool for the gynecologist because it allows examination of the female internal genitalia that is more accurate than bimanual examination and less traumatic than laparotomy. A few patients will always benefit by such an examination. Its use in female sterilization is certainly acceptable but may be replaced by simpler methods in the future.

Carl E. Johnson, M.D.*
Rochester, Minnesota

*Section of Obstetrics & Gynecology, Mayo Clinic.

Spontaneous Healing of Interventricular Septal Defects

TRAUMATIC RUPTURE of the ventricular septum secondary to nonpenetrating chest trauma is an uncommon but well-recognized entity. In the April issue* Drs. Goldfarb and Wang present an interesting case of a 20-year-old man who developed a traumatic ventricular septal defect following severe chest trauma in an automobile accident. Attempted surgical closure of the defect approximately three months after the accident was apparently unsuccessful, but a spontaneous reduction in the degree of shunt was documented over the next two and a half years.

In their case no murmur of a ventricular septal defect was heard in the first five days after the accident, but one was present on re-evaluation two weeks later when the patient was admitted to the hospital with pulmonary edema. A delay in the appearance of a typical murmur is a frequent occurrence in traumatic ventricular septal defect and suggests that the septum, first contused, becomes necrotic and finally perforates. In one report describing a traumatic ventricular septal defect repaired 12 days after injury, the margin of the defect was found to be softened and necrotic.[1] Further evidence that this sequence of events occurs is the frequent association of either electrocardiographic changes of an anterior or inferior myocardial infarction, or the subsequent development of a ventricular or septal aneurysm, or both.

Such findings suggest that the surgical treatment of a traumatic ventricular septal defect should be similar to that of a postinfarction ventricular septal defect,[5] i.e., postponing repair for at least three months, and preferably longer, unless clinical deterioration occurs in spite of intensive medical therapy. The ideal time for repair of a ventricular septal defect after myocardial infarction, or traumatic ventricular septal defect, appears to be three and a half to six months on the basis of the work of Mallory and associates.[3] The high incidence of residual or recurrent shunts (six out of 12 patients in one review[1]) is similar to that for repair of postinfarction ventricular septal defect,[5] and suggests that operation should be delayed for fibrotic healing of the margins of the defect.

Most traumatic ventricular septal defects occur in the muscular portion of the septum near the apex, and more than one perforation is common. Single perforations of the septum may appear multiple, when viewed from the right ventricle, because of the dense network of trabeculae at the apex. Excision of the trabeculae before attempting closure of the ventricular septal defect aids in achieving an accurate repair.

If a ventricular aneurysm is present in the left ventricle, it is desirable to incise it and repair the septal defect from the left side, as suggested by the authors. The aneurysm can then be resected as indicated during closure of the ventriculotomy.

The authors propose waiting for spontaneous healing of the septal defect, on the basis of their case and one recently reported in the literature,[4] as a nonoperative alternative to surgical closure. Spontaneous healing does occur, but the percentage of traumatic ventricular septal defects that heal spontaneously is probably small. On the basis of these two cases, followed three and a half years and eight years respectively, the time for spontaneous healing would appear to be several years. Both of these patients still have residual shunts. Of the nine patients treated medically since surgical means of closing the defect have

*See page 325.

become available, five have died,[1] two from cardiac arrhythmia, one from multiple injuries, and two from a persistent large left-to-right shunt. No deaths have yet been reported among the 12 patients treated surgically.[1] Our preference is, therefore, surgical closure of all large traumatic ventricular septal defects which still appear to be hemodynamically significant after observation for a suitable period of time, four to eight months. Further experience in the treatment of these lesions, combined with careful hymodynamic assessments such as those reported by Goldfarb and Wang, will be needed before the best plan of management can be definitely known and agreed upon.

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†Department of Surgery, Mayo Clinic.

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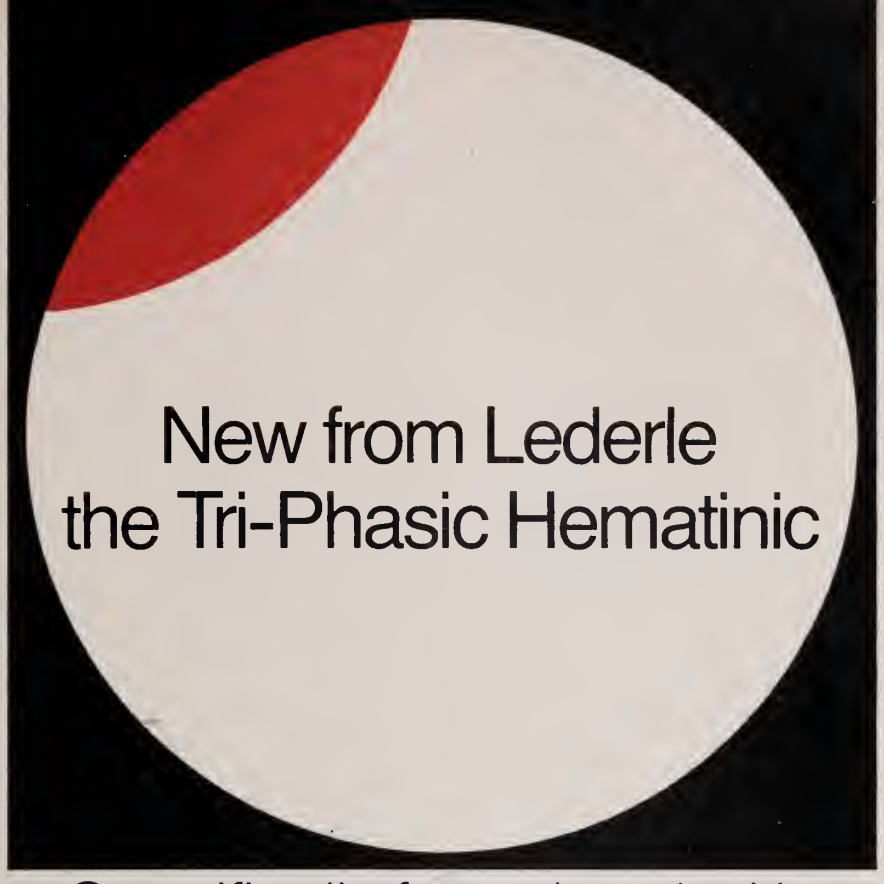
Florida to Issue Medical Licenses by Endorsement

EFFECTIVE SEPTEMBER 1, 1971, for the first time in history, the Board of Medical Examiners of Florida may issue licenses by endorsement to practice medicine and surgery in Florida. An amendment to the Medical Practice Act of Florida, enacted by the 1971 legislature allows issuance of licenses by endorsement to those M.D.'s who have been certified by the National Board of Medical Examiners or the Federation Licensure Examination (FLEX) within a period of eight years preceding the date of application for license by endorsement.

Since the effective date is September 1, 1971, this means that an M.D. must have been certified by the National Board of Medical Examiners since September 1, 1963, in order to initially be eligible for licensure by endorsement. As far as other state licensure examinations are concerned, this amendment only applies to those states who use the Federation Licensure Examination (FLEX) as their licensure examination.

In the case of foreign medical graduates, this does not eliminate the requirement that the M.D. have papers of first intention of citizenship and a minimum of one year's residency in the United States and the Educational Council for Foreign Medical Graduates Certificate of proficiency. A very important feature of the amendment is the provision that a physician who receives a license by endorsement in Florida must practice in the state within a period of three years for a minimum period of one year. If he does not do this the license will become null and void. Service in the armed forces is exempt during these three years, but internship or residency time is not exempt.

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Laboratory Letter

Screening for β- Hemolytic Streptococcus In the Throat

Charles W. Jarvis, M.D.*
St. Paul, Minnesota

IDENTIFYING SORE throat of group A, beta hemolytic streptococcus is difficult enough so that many laboratory procedures have been devised to aid the clinician. The best procedure involves culturing material from the oropharynx on blood agar; isolating a small colony that produces a zone of clear hemolysis; examining the colony by gram stain to rule out other beta hemolytic organisms; and finally subculturing followed by serological identification of the Lancefield group.

This method is time consuming and expensive for the usual sore throat. Another method has received publicity because of its rapidity. This is the fluorescent antibody tagging of four-hour-old cultures. Unfortunately this is not conveniently available for most physicians and their patients.

There remains a third method, really just a simplified version of the first, that requires a minimum of handling, equipment, bacteriological expertise, and time, This method has become popular in physicians' offices and outpatient departments because it is rapid and inexpensive. The procedure is as easy for the physician in a one or two girl office as for the physician in the big clinic and as useful to a small town generalist as to the big city pediatrician.

Material

Blood Agar Plates

Use trypticase soy agar with 5-10% sheep blood in sterile, disposable plastic Petri plates. Sheep blood is preferable to human (outdated blood-bank) blood because the latter may inhibit the growth of streptococci. Ready-made plates are available from numerous commercial sources, but since freshness is important, many physicians purchase a few plates at a time from the nearest hospital bacteriology laboratory where a high use rate usually will guarantee that the agar will not dry out before it is used.

Incubator

There are a number of small incubators available from laboratory supply houses. Be sure there is adequate temperature control because these organisms grow best at a temperature slightly below 37°C.

Cotton tipped applicators.

Bacitracin discs, 0.04 unit†

Procedure

1. Swab the inflamed area of the pharynx. Try to avoid contamination by the tongue and saliva.
2. Rub the applicator over the surface of the blood agar, using overlapping strokes (Figure 1). Use about half the plate. If supplies are scarce, two patients can easily occupy one plate.

---

*From the Department of Pathology, Childrens Hospital, St. Paul, Minnesota.
Correspondence to: Childrens Hospital, 311 Pleasant, St. Paul, Mn. 55102
†Taxo A Sensi-Disc, BBL, Cockeysville, Md.



Fig. 1—Rub the throat swab over the blood agar in overlapping strokes.



Fig. 2—Place a 0.04 unit bacitracin disc in the center of the area which has been swabbed.



Fig. 3—Positive screening culture. The dark ring around the black disc represents a zone of unhemolyzed blood where bacitracin-sensitive bacteria can not grow. They grow well elsewhere and produce clear (beta) hemolysis. The bacitracin-resistant organisms which grow in the dark ring do not produce hemolysis.



Fig. 4—Negative screening culture. The homlytic bacteria grow well right up to the bacitracin disc because they are resistant to the action of the bacitracin.

3. Place a bacitracin disc on the swabbed surface and push gently to be sure it has made firm contact with the agar (Figure 2).
4. Incubate at 35-37°C for 18 hours. The 18 hours allows plenty of time for good growth and hemolysis to take place but longer times (such as from Saturday noon to Monday morning) are acceptable.

Interpretation

Read the plate for bacitracin sensitivity and beta hemolysis (Figure 3). Remember that the group A, beta hemolytic streptococci form small, white colonies which produce clear (beta) hemolysis in the blood, and will not grow to within 15-20 mm of a bacitracin disc. Green (alpha) hemolysis indicates some other streptococcus or pneumococcus. Other colonies with beta hemolysis, but which are resistant to bacitracin, will be non-group A streptococci, hemophilus, or even colon bacilli. Any of these will produce a picture like that in Figure 4.

There you have it. There are many refinements that you can add, of course, but this simple system will give you an answer—an answer obtained with minimal expenditure of patient funds and physician effort, but one obtained rapidly enough so that you can wait for it before deciding that a 10-day-long course of penicillin is indicated.

Trained Laboratory Technicians

For many years it has been difficult for physicians to hire adequately trained laboratory technicians to work in their offices, especially if the physican practiced alone or in a small group where the volume of lab work was not great, or practiced in a rural community when the social opportunities were limited. In an attempt to solve this problem, the Minnesota Society of Clinical Pathologists and the Minnesota Society of Medical Technologists formed a Medical Laboratory Assistants (MLA) Board to help start training courses for medical laboratory assistants, and to guide the education of these students. The Board is composed of pathologists, medical technologists, and certified laboratory assistants, all of whom serve without pay. At the present time, there are five schools which have been inspected and approved by this Board. They accept upper level high school graduates for training periods varying from 12 to 24 months. Their courses include chemistry, urinalysis, hematology, serology, blood banking, EKG, and some basic bacteriology. In addition, they learn basic quality control procedures and are constantly reminded that the patient is the only reason for the profession's existence. The graduates take a certifying examination given by the MLA Board. The young adults who graduate from the courses in these five schools are well trained and capable of doing the basic tests needed in most physicians offices.

More information on the MLA courses or on the availability of graduates contact one or more of the following sources directly.

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Fracture Conference

Birth Fractures*

ANTHONY J. BIANCO, M.D.,† ALLEN P. SCHLEIN, M.D.,† ROBERT L. KRUSE, M.D.†
EINER W. JOHNSON, JR., M.D.†

Robert L. Kruse, M.D.:

Osseous injuries in the newborn are usually secondary to birth trauma, congenital fragility, osteogenesis imperfecta, or congenital pseudarthrosis of the tibia. We will discuss the problem of birth trauma.

Time may be an important factor in delivering an infant in breech presentation, and the obstetrician may deliberately fracture the clavicle or the humerus in problem deliveries. The clavicle also may be broken by a shoulder dystocia, especially when the infant is unusually large. Osseous injuries obviously are of less consequence than prolonged cerebral anoxia. About three fourths of birth fractures occur in breech presentation. In the usual case, the mother is a primipara and, surprisingly, the infant is not extremely large.

With proper diagnosis and adequate treatment, the prognosis for these injuries should be excellent. The infant has a marked ability to form callus and to heal fractures. Nonunion is practically unheard of, and union occurs rapidly. Angulation is usually remodeled within the first two years of life.[1]

The diagnosis of a birth fracture is easy if one knows the features of skeletal development and the manner in which the periosteum and the soft tissue react to trauma. Fractures of an extremity are usually complete and have considerable displacement. The first evidence of injury may be the tumor of callus formation, appearing one to two weeks postpartum, but callus formation can often be seen on roentgenograms as early as the fifth day.

Obstetric palsy can be confused with clavicular or humeral fracture or can mask a fracture in this area.[2] The shaft of the long bones is involved more commonly than the epiphysis. Clavicular fracture is the commonest injury. In Madsen's study[3] of 105,119 newborns, 726 fractures involved the clavicle.

*Fracture Conference, July 7, 1969.

†From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Types of Injuries

Clavicular fracture usually involves the middle third of the shaft and usually is of the greenstick type (other types of birth fractures are usually complete fractures). This fracture is generally secondary to digital pressure on the clavicle during delivery and to attempts to deliver the aftercoming head in a breech presentation. In a vertex presentation, traction or shoulder dystocia causes fractures in this region. Treatment may not be necessary, but the infant is often placed on its back with a small folded towel between its shoulder blades.

Humeral fractures usually occur in the middle third of the shaft and are either transverse or spiral. The anterolateral angulation of the proximal fragment is commonly caused by the deltoid muscle. This is because the fracture is just below the insertion of the deltoid on the humeral shaft. This injury can be complicated by radial palsy, but this generally disappears within six to eight weeks. The mechanism here is usually traction on the extended arms in breech presentations. Also, in cephalic presentations, fracture of the humerus may be caused by the use of axillary traction to disengage an impacted shoulder. Treatment again should not be strenuous. The arm can be abducted on an axillary pad and also strapped to the chest. This axillary pad brings the distal fragment into abduction with the proximal fragment. Shortening and angulation up to 40° to 50° will be corrected within two years.[1]

Femoral shaft fractures occur in the middle third and are transverse. The proximal fragment is abducted and flexed by the psoas muscle so that it will be at right angles to the distal fragment. This injury is caused by torsion on the legs in breech delivery. Also, groin traction or bringing the leg down from the extended breech position can result in fractures of the femur. This fracture should be treated by Bryant's traction which will bring the distal fragment into a flexed

position and in relationship to the proximal fragment. Overriding of 1 cm and 20° of posterior angulation are reported by Madsen[3] to be acceptable.

Periosteal stripping and epiphyseal displacement are the last injuries which we will discuss. Periosteal stripping is manifested by pain and swelling in the traumatized area, associated initially with normal roentgenograms. After five to seven days, subperiosteal calcification appears on the roentgenogram. If injury to the periosteum is associated with epiphyseal displacement, the greatest mass of subperiosteal calcification will be seen in the area of the epiphysis. Snedecor and Wilson[4] found that in approximately 6% of 50 consecutive breech deliveries there was subperiosteal calcification within five to seven days after birth.

Epiphyseal displacement usually occurs in the distal part of the femur or the upper or lower part of the humerus. Trauma in relationship to breech extraction is the usual cause. Diagnosis is made by physical examination, often associated with a history of the bone audibly cracking or the shaft giving way during delivery. Ferguson[5] reported that all epiphyseal displacements are associated with a fracture (triangular) of the metaphysis—the so-called Thurston-Holland sign which may be seen on the roentgenogram at birth. Displacement is usually absent or minimal but, if displacement occurs, gentle manipulation and splinting is the treatment of choice.

The lower femoral epiphysis is roentgenographically evident at birth and, if it is displaced, it usually will be so posteriorly. Treatment is by Bryant's traction for two to three weeks. If manipulation is necessary, one has to be careful to avoid compression of the popliteal vessels. If slipping of the distal femoral epiphysis is not corrected at birth, the hematoma will form a new shaft posterior to the original shaft and the latter will be absorbed. Remodeling of this deformity will take two to three years, but it will correct itself.

Upper femoral epiphyseal displacement is a rare birth injury. When it occurs it is also treated by Bryant's traction. Baron and associates[6] recommended spica casting for six weeks, but I do not think that this is necessary. I believe Bryant's traction to be satisfactory treatment for most femoral injuries. As coxa vara and degenerative changes occur secondary to this type of injury, the parents should be informed of possible complications.

Lower and upper humeral epiphyseal displacements are treated primarily by sling immobilization, with the elbow in 90° of flexion.

Illustrative Cases

Allen P. Schlein, M.D.:

We have three simple cases to present, demonstrating some of the things that Dr. Kruse has discussed.

The first patient was born here in December 1967, without any specific history of difficulty occurring during delivery. He was circumcised and dismissed from the hospital as a normal, newborn infant. However, on December 30, 12 days after birth, he was returned to the emergency room by his mother because she had found a large, mildly tender mass over his left clavicle. Careful questioning of the mother revealed that the child had had a bruise in the area shortly after delivery. Roentgenograms taken in the emergency room revealed a healing fracture of the left clavicle (Figure 1). This simple case was chosen to show that the first sign of a birth fracture can be the large, exuberant callus found two weeks after the injury.



Fig. 1 (Case 1). Callus is present secondary to healing of fractured left clavicle.

The second patient had been born after a difficult breech delivery, and the obstetrician immediately recognized the fact that the humerus had been fractured (Figure 2). The child was placed in a swathe to hold the arm to the side. There



Fig. 2 (Case 2). Transverse fracture of midshaft of right humerus of newborn.

was no neurocirculatory problem.

Anthony J. Bianco, M.D.:

Dr. Mess, do you think this fracture would be difficult to immobilize?

Charles F. Mess, M.D.:

I think it would. All the parts are so small that it would be difficult to wrap the child. There also are many problems in the care of the child, such as bathing, diapering, and so forth. However, I would try to immobilize it close to his side as was mentioned.

Mark B. Coventry, M.D.:

I would disagree. I would leave it strictly alone and would not try to strap it, as it then becomes virtually impossible to bathe the child. We all know that it will heal perfectly if we leave it strictly alone, so why strap it?

Dr. Bianco:

But don't you think that, when the child is fussy for the first few days, it is a simple matter to immobilize the fracture at the side until the region needs cleansing?

Dr. Schlein:

After this child was sent home, he was never even returned for another roentgenogram and he never had any difficulty with the arm.

Dr. Mess:

Have radial nerve injuries ever been reported?

Dr. Bianco:

I personally have never seen one in a fracture in the newborn. I think it would be hard to diagnose and is probably missed.

Henry N. Goodwin, M.D.:

If you just left these fractures alone, would not the chance of radial nerve injury be increased?

Dr. Bianco:

You would think so, but letting them alone does not seem to increase the number of radial nerve injuries.

Dr. Schlein:

The third case demonstrates a slightly different problem in a breech delivery. This baby weighed nine pounds 11 ounces at birth here in February 1966. The mother was known to be diabetic, and this was her first child. Labor was slightly prolonged and delivery was reported as difficult. It was noted that the child did not move its left arm, and a roentgenogram taken at that time showed a transverse fracture of the left humerus (Figure 3-A). This was treated by binding the arm to the chest with a swathe for a period of three weeks. However, a roentgenogram made nine days after injury (Figure 3-B) showed surprisingly little callus; but roentgenograms one month after injury (Figure 3-C) showed that the fracture was healing well with minimal treatment.

Joseph M. Janes, M.D.:

I would like to mention a case in which a boy, whom I saw when he was nine years old, had had a birth fracture of the midshaft of the femur.

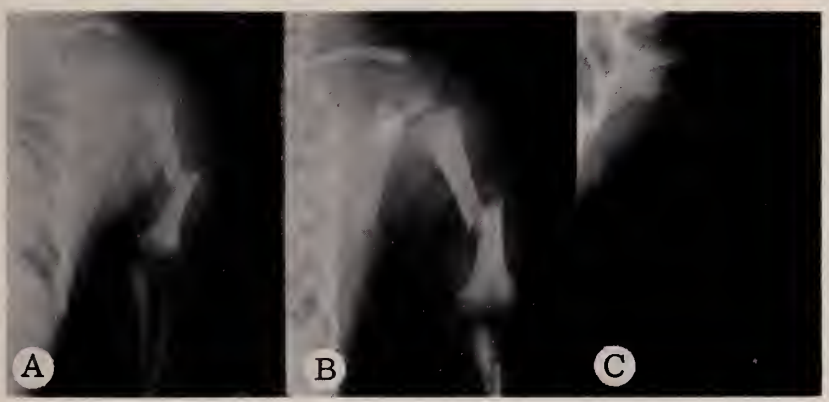


Fig. 3 (Case 3). (A) Transverse fracture of left humerus, at birth. (B) At nine days after injury. (C) Healing fracture approximately one month after injury.

It was in good position, but the extremity was shortened one and one-half inches. Obviously not all these problems correct themselves.

Dr. Bianco:

That is a good point. We are talking about birth fractures in otherwise normal infants, not about osteogenesis imperfecta or congenital pseudarthrosis of the tibia. We know that these fractures should heal in rapid fashion regardless of the treatment. I was going to ask the consultants if they ever have seen a nonunion of a birth fracture.

Dr. Coventry:

I may have such a case. The child was not born here, but the history from the mother and the local physician indicates that it probably was a birth fracture. Of all things, it was a clavicular fracture, and it did not unite. We have roentgenograms covering two years, from at least three months postpartum. The child had no characteristics of congenital pseudarthrosis. This was a strange case, and I had to do a bone graft when the child was two years old. It did go on to union. This conceivably could have been a postpartum fracture.

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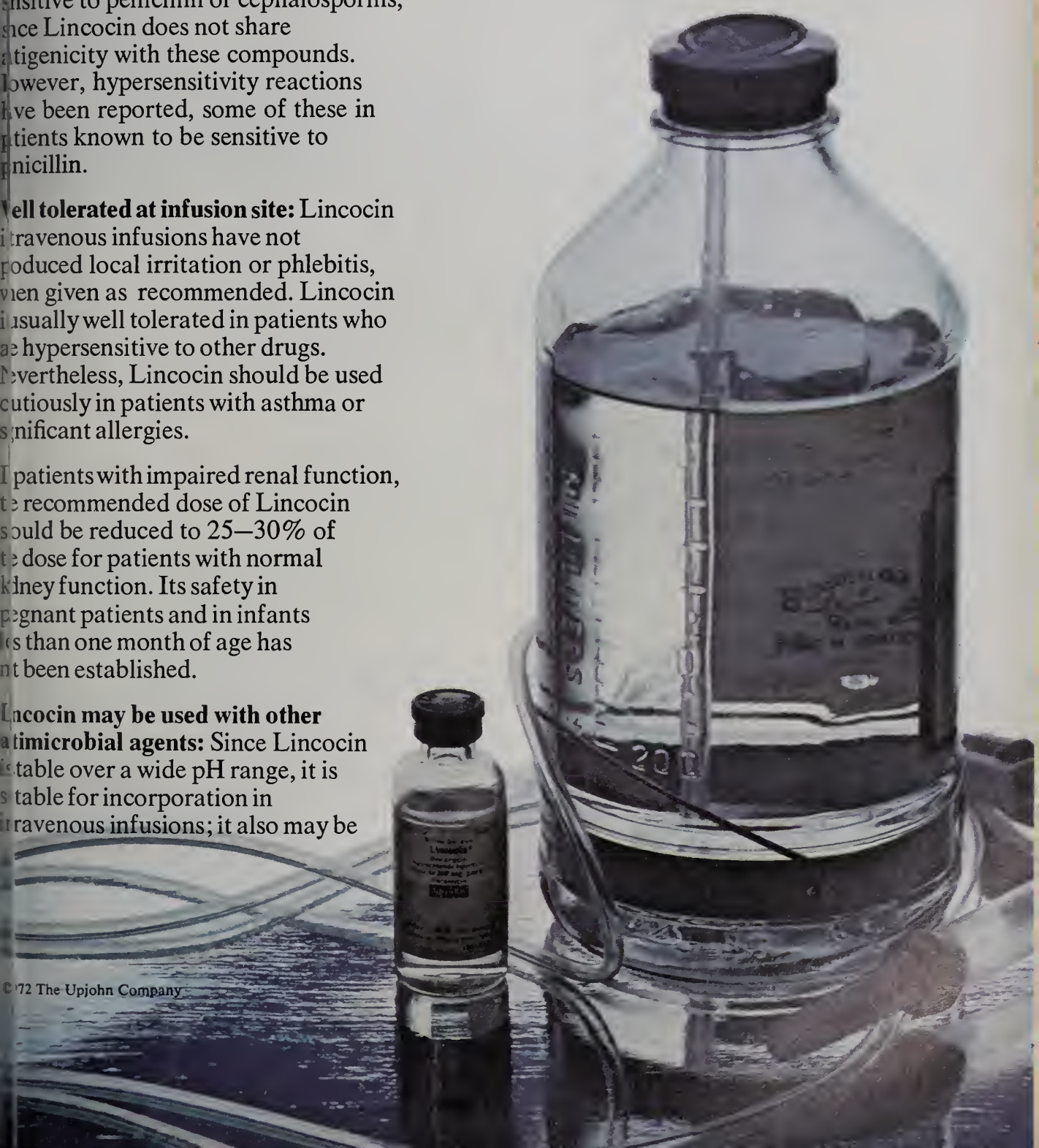
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ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatm *Skin and mucous membranes*—Skin ra urticaria, vaginitis, and rare instances o foliative and vesiculobullous dermatitis been reported. *Liver*—Although no direc lationship to liver dysfunction is establis jaundice and abnormal liver function (particularly serum transaminase) have observed in a few instances. *Cardiovasc* —Instances of hypotension following pa teral administration have been repo particularly after too rapid IV admini tion. Rare instances of cardiopulmonar rest have been reported after too rapi administration. If 4.0 grams or more ad istered IV, dilute in 500 ml of fluid administer no faster than 100 ml per h *Special senses*—Tinnitus and vertigo been reported occasionally. *Local reac* —Excellent local tolerance demonstrate intramuscularly administered Linc (lincomycin hydrochloride). Reports of following injection have been infreq Intravenous administration of Lincoc 250 to 500 ml of 5% glucose in dist water or normal saline has produce local irritation or phlebitis.

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Fetal Monitoring*

A Retrospective Evaluation

DAVID L. HILL, M.D.†

MODERN OBSTETRICS has come to recognize the dynamic nature of labor and its inherent stresses on the fetus. With electronic advancement, fetal monitoring has become available to all major obstetrical services, and much enthusiasm has been generated for this method of evaluating fetal stress. Because many of the variations in fetal heart rate and intrauterine pressure are only detectable by constant monitoring, many presume that best obstetrical care can be given only with this method of detecting early fetal stress and determining which of the variations are benign. The questions raised at this point are many, but a few warrant emphasis. What is the expenditure of time required by the staff to operate a monitoring unit? How often is the monitor able to add to information already known by standard observation methods? How difficult are records to interpret? How reliable is the monitor in predicting distress? Is fetal monitoring a practical method for all hospitals at this point in its development?

*Paper and discussion presented to the Minnesota Society of Obstetrics and Gynecology, April 24, 1971, Duluth, Minnesota.

†Department of Obstetrics and Gynecology, Hennepin County General Hospital, Minneapolis, Minnesota.

Materials and Method

The present study is a review of the first one hundred patients monitored at Hennepin County General Hospital. From March, 1970, to January, 1971, 1,524 infants were delivered at the hospital. Of these 100 or 6.5% were monitored. The reasons for monitoring are listed in Table 1. The

TABLE 1
Reasons for Monitoring

Premature Rupture of Membranes	32
Toxemia	20
Secondary Arrest	18
Fetal Heart Rate Irregularity	15
Cephalo-Pelvic Disproportion	15
Primary Dysfunctional Labor	14
Meconium Stained Fluid	14
Postmaturity	7

60% Oxytocin Stimulation
14% Failure Rate

TABLE 2
Results of Review

	Distress by FHR	Low Apgar Score	Cesarean Section
Fetal Heart Rate Patterns			
Tachycardia (32)*		6	5
Late Decelerations (4)		2	2
Severe Variable Decelerations (10)		2	2
Contraction Patterns			
Incoordination			
Primary (33)	13	5	3
Secondary (5)	3	2	0
Hypertonus (30)	13	3	3
Tachysystole (17)	8	2	2
Hypersystole (13)	7	1	3
Meconium Stained Fluid (14)	9	2	5

*Total patients in group in parenthesis.

Corometrics FMS-101 Unit* was used. Residents in obstetrics hooked up the monitor and followed these patients. The results were used for clinical decisions. All records were reviewed and classified after delivery. Variant patterns of both fetal heart rate and intrauterine pressures were compiled in various categories according to Caldeyro-Barcia[1] and Hon[2] (Table 2). The outcome of each labor is very difficult to evaluate, but the parameters chosen were fetal distress (defined as tachycardia, late decelerations, or severe variable decelerations), low Apgar scores (< 4 at 1 minute or < 7 at 5 minutes), and cesarean section rate.

Of special interest was a review of obstetric statistics comparing Hennepin County General Hospital with Northwestern Hospital. Northwestern Hospital is a private Minneapolis hospital with 25% fewer deliveries than General Hospital. All patients at Northwestern Hospital were followed and delivered by obstetricians but fetal monitoring equipment was not available. Comparison of perinatal mortality, cesarean section rate and low Apgar scores in these two hospitals are made in Table 3. Also included for comparison are the statistics for the year immediately preceding the installation of monitoring equipment at General Hospital.

TABLE 3
Comparative Statistics

	HCGH 1969	HCGH 1970	NWH 1970
Perinatal Mortality*	44	31	18
Corrected (> 2,500 gms)	10	5	2
Cesarean Section Rate	5%	6%	10%
Low Apgar, Score	†	6%	3%

*Per 1,000 live births.
†Information not available.

Results

Conclusion must be drawn with caution from such small groups as these with so many variables. The limitations in the interpretation of retrospective statistics must also be kept in mind.

Personnel and Interpretation

At General Hospital, there is 24-hour staffing by residents in obstetrics. As the monitoring program progressed, it became obvious that this full-time coverage was absolutely necessary. Not only do problems arise at any hour of the day, but there must be someone with experience to apply and maintain the equipment, as well as interpret the records. Interpretation of records is not a simple matter, because changes are frequently combinations of different patterns. Attempts to use the monitor failed in 14% of the patients, due to faulty scalp electrodes or inability to pass the intrauterine catheter.

Fetal Distress by Fetal Heart Rate

Parameters of fetal distress occurred in 46% of the total patients. The most frequently observed parameter was tachycardia. It responded to treatment by position change and maternal oxygen. If oxytocin was being administered, it was decreased or discontinued. The other types of fetal distress also responded to treatment in most cases. Only four patients were finally delivered by cesarean section.

The majority of irregular fetal heart rate patterns were variable decelerations, a variation that can be diagnosed only by continuous monitoring. Because this abnormality is known to be a benign pattern, except in its severest form, operative intervention was prevented in several cases.

Abnormal Contraction Patterns

In the total group of 100 patients, 60% received intravenous dilute oxytocin for stimulation or induction of labor. This must be considered when interpreting the results to follow.

Hypertonus was observed in 30% of the group, many times in a very subtle way that would not have been detected except by a monitoring service. Clinically a significant increase in the baseline pressure was not always accompanied by painful or palpably hard uterine contractions. On one occasion, an oxytocin overdosage was detected immediately with no resultant harm to the fetus. This infrequent, but real situation, is safeguarded by the monitor. On the other hand, oxytocin can be increased with safety more rapidly to an effective level saving time with inductions. An earlier diagnosis of failed induction can also be made if exact contraction patterns are known.

Incoordinate contraction patterns were observed in 38% of the patients studied. Monitoring makes this pattern more easily recognized, and appropriate treatment can be given earlier.

Low Apgar Scores

A low Apgar score was defined as less than four at one minute or less than seven at five minutes. By these criteria, fourteen infants had a low Apgar score in the study. Only 50% of

*Corometrics Medical Systems, North Haven, Connecticut.

these were predictable by the monitoring record because the record was not available up to the time of delivery. It is generally accepted that the fetus can get in or out of trouble within 20 to 30 minutes.

Of the fourteen infants, eight were delivered by cesarean section. Because of this, there were additional factors that could have contributed to the low Apgar scores, especially at one minute.

Cesarean Sections

Fifteen patients were delivered by cesarean section. In most of the sections the deciding factor for operative intervention was the contraction pattern. In four other cases the fetal heart rate indicated fetal distress. These findings tend to shift the emphasis in monitoring from the fetal heart rate pattern to the uterine contraction pattern. This is logical because fetal distress is almost always related to stress secondary to the uterine contractions.

Hospital Comparisons

If the statistics at General Hospital are compared (Table 2) for the year before and the year of monitoring, the difference is striking. Although many factors are involved, one concludes that monitoring may have played an important role in decreasing the corrected perinatal mortality by 50%. The similarity of cesarean section rates may indicate better selection for operative intervention.

When the applicability of fetal monitoring is considered for any particular obstetrical service, the statistics of that service must be reviewed. Some services have results that would be difficult to improve. This seems to be the case at Northwestern Hospital but the price paid is a 10% cesarean section rate. The expenditure of time and money for monitoring in this situation cannot be justified.

Discussion

In the evaluation of a new method or technique, it is important to remember the basic principles involved. Monitoring is simply a graphic display of the stress of uterine contractions on the fetus, which may lead to hypoxia and acidosis, resulting in changes in the fetal heart rate. In other situations, contractions exert to pressure on the cord or head which leads to changes in the fetal heart rate. This review indicates the frequency of abnormal contraction patterns, and helps to emphasize the importance of intrauterine pressure. Not enough emphasis has been placed on contraction patterns, which leads to a pessimistic viewpoint in thinking that external monitoring will ever have anything to add, except in the area of stress tests.

Conclusion

Fetal monitoring gives the obstetrician more objective data to assist him in making clinical judgments. It is also an aid in teaching. In some circumstances, monitoring appears to definitely improve the statistical outcome of pregnancy. There are some[3] skeptics who suspect that the major factor in improvement on statistics results from the closer attention given by the staff.

For some obstetrical services, the time, training and expense, make monitoring impractical or impossible to obtain and operate efficiently. For others, monitoring may be unnecessary.

At the present time fetal monitoring is confined to the teaching obstetrical service. It may become applicable to the population at large only when obstetrical services combine to make an obstetrical intensive care unit a reality.

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Meetings

American Medical Writers Association

The North Central Chapter will sponsor a workshop "To Improve Medical Writing," May 13, 1972, Mayo Building, 15th Floor Lecture Hall, Rochester. Fee: $25.00. Registrations to: Eleanore Clappier, Proceedings Office, Mayo Clinic, Rochester.

Discussion

Donald W. Freeman, M.D.:

Dr. David Hill has taken a look at some of the problems involved in electronic fetal monitoring together with the expected yield, and has set forth some of the arguments for and against its application in private non-teaching hospitals. I think that he has done this well and fairly. I also think it is an appropriate thing to do since, after all, the vast majority of babies born in Minnesota and in the country are delivered by private practitioners in private hospitals. I would like to offer these comments.

Each month at department meetings, we review the circumstances relating to labor and delivery with regard to all babies born with depressed Apgar scores. We always find some that are unexplained. This suggests that something occurred that was missed by ordinary clinical observation, because it has been shown that if fetal heart rate patterns are normal up to within twenty or twenty-five minutes of delivery, 99% of the babies are in good condition. My conclusion on this first point is that we should, at General Hospital, be doing more monitoring than we are. Reports from elsewhere suggest that 20% to 30% of deliveries might be an optimal number depending on the frequency with which oxytocin induction and/or stimulation is used.

I think everyone agrees that in private practice, the numbers of high-risk pregnancies and the numbers of patients who require monitoring is proportionately a good deal lower than at Hennepin County General Hospital. Nevertheless, every private service has some candidates. The differences are only in percentages.

It also seems generally agreed that monitoring detects evidences of fetal distress that ordinary observation of labor and auscultation of fetal heart tones will not, and that monitoring, furthermore, can pick up signs of distress very early in the course of its development. When detected such early distress can be treated in utero by administration of oxygen to the mother, position change, discontinuance of oxytocin if it is being given, taking measures to elevate the blood pressure if there is a blood pressure drop, and if it is indicated, termination of the labor. Such early detection and early treatment minimizes the time during which the fetus is distressed. Simple logic would suggest that this has to be good.

Monitoring in other institutions has provided a substantial reduction in the numbers of cesarean sections done for fetal distress. Furthermore, it probably reduces the number that are done for certain other conditions, such as disproportion, diabetes, toxemia, abruptio, etc. As long as the fetus in these high-risk patients remains in good condition as manifested by heart rate patterns, labor or trial of labor can be allowed to proceed—often to vaginal delivery. On the other hand, if we were not so sure of the safety of the labor to the patient and fetus, we might be tempted to terminate it by cesarean section.

Finally, I agree that the costs in terms of time expended by trained people is high. A physician has to be there to do the hookup, to watch the equipment, and to interpret the tracings. Furthermore, it takes some special training to do this. All in all, I am inclined to agree that it is probably impractical to get monitoring done in most private hospitals as *obstetrics is now practiced,* and furthermore, that the expected yield would be relatively small. On the other hand, I think that monitoring is here to stay, and that more of it should be done. What then is the solution?

It may be that some redistribution of manpower is required. Perhaps obstetrics should be practiced by groups of physicians which will allow completely adequate hospital coverage and utilize paramedical personnel for many of the things that obstetricians now do in their offices. Many hospital obstetrical services that are small and inefficient should be closed. Larger concentration of patients will bring larger numbers of high-risk problems and make more feasible the provision by the hospitals of adequate services, including house staff, monitoring equipment, qualified anesthesia, newborn intensive care units, etc. Finally, I believe that where circumstances don't permit development of facilities big enough to accomplish this, that high-risk obstetric patients should be referred to a center which can provide such services.

Special Article

The Changing Face of Medicine*

RAYMOND J. JACKMAN, M.D.†

I WAS A MEMBER of this House of Delegates some 25 years ago, and I should like to share with you for a few minutes some of the changes that have taken place since that time. In the era of which I speak, the doors to deliberations of this House of Delegates, for the most part, were closed to the news media. Medicine shunned publicity with a passion.

Medicine and the Media

Then, after years of knocking on the door, Victor Cohn, a science writer for the *Minneapolis Tribune*—now with the *Washington Post*—was admitted, tentatively at first, and was soon found to be friendly to medicine. Gradually he was welcomed warmly, as were other newspapermen and writers. That was in the 1930's and 1940's, a time when personal reticence and humility in physicians were thought commendable, and anything that smacked of self-advancement was considered unethical. The public's growing interest in science and medicine, the news media's effort to meet the public interest, and the willingness of some scientists to step into the public spotlight have produced a situation which appears to be steadily worsening or bettering, depending on your point of view.

Private Practitioner and Publicity

Today it would seem that only the private practitioner is denied the doubtful privilege of self-display. There are those who say the power of fame and money is effacing the tradition of good taste which physicians had thought important but which is more often contemptuously dismissed by some of the public as "hypocrisy." They would make the physician's behavior no different from that of anyone else.

Recognition

It is true that no human trait is stronger than the desire for recognition. It is the most potent, if not the most laudable, stimulant to achievement. Like it or not, the desire for approbation is an integral part of the human scene, and no amount of mock humility will rid us of it.

As I think back about 40 years ago, when I was graduated from medical school, changes that have occurred in physicians' behavior are really incredible. When I began to practice, conformity was the order of the day; now the complete opposite is true. The public now calls medical dignity "pretension," and quarrels between two of our internationally known surgeons are front-page news, even in the conservative WALL STREET JOURNAL.

Ego has to be the central phenomenon of the Twentieth Century, even if patriotic Americans pretend it does not exist in their heroes. The most monstrous exhibition of ego in a brave man in many a year was Alan Shepard's three whacks at a golf ball while standing on the moon. There, in a space suit and hardly able to stand, he put a club head on an all-purpose tool and, restricted to swinging with one arm, he dubbed the first two shots, but on the third in a low gravitational field the ball went a half mile.

Television as a Force

Have you ever sat back and reflected on what powerful forces the news media, and particularly television, are? Big-league football games are, and even the launching of Apollo 14 was, scheduled for prime viewing time. Even the agitators hold off, if they can, to do their "thing" until the television camera is pointed at them. In your wildest dreams 20 or 30 years ago, could you picture a presumably noted surgeon performing the very experimental heart transplant before the eye of the television camera, telecast to the

*Presidential Address to the House of Delegates, Minnesota State-Medical Association, St. Paul, Minnesota, May 16, 1971.

†Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

public from coast to coast? In your wildest dreams of years ago, could you picture individual citizens with no medical or scientific background debating in news media or before Congressional committees the merits or demerits of the "pill," marijuana, and even LSD? And guess who said this, "Since the advent of heart pacemakers and catheterization, the hospital environment has become so dangerous that today it is the site of more electrical accidents than any industry except mining."

Order of the Day

Change and innovations seem to be the order of the day, as they have always been, and the public, the consumer—call him what you will—is here to stay and is very much involved in things medical. From the point of view of the public, there is nothing sacred about solo practice, and there is nothing unethical about having a physician accept a yearly salary from a third party, be it an insurance company or the federal government, rather than a fee for service.

Rising Costs

The rising costs and unsatisfactory state of medical care have finally gotten just about everyone impatient to see a change, and at present there are at least eight bills affecting the nation's medical care being debated by our national legislators. Both major parties are participating in one way or another. Some of the plans, like Senator Kennedy's, are visionary and extreme; some, like the President's and the American Medical Association's Medicredit, are more conservative. But you should be prepared —like it or not, deep change is coming.

Malpractice Dilemma

The major questions which physicians must help the public answer are those related to how people can obtain the best health care at costs that can be borne. But since the consumer has entered into systems of health-care delivery, he also should be brought face to face with vexatious problems such as the "malpractice dilemma."

The rapid increase in money awards against physicians arises from the fact that many suing patients and many jurors entertain the opinion that physicians make too much money from their practice. The threat of malpractice litigation dramatically affects the practice of medicine. Physicians indeed, and for good cause, are becoming supercautious in an effort to protect themselves. They are practicing defensive medicine. They have been forced into a position which compels them to order extra tests and xrays so that the record will show that their ministrations were conscientious; they keep patients in hospitals longer to ensure that treatment will be considered adequate, and they avoid risky diagnostic procedures and ignore new treatment techniques for fear of accusations of resort to unnecessary methods.

Costs of Liability

Physicians have to pass on the high costs of liability to their patients. If the patient-consumer is going to involve himself in things medical, medicolegal disputation is one area in which he should be encouraged to enter.

For instance, the contingency fee has paved the way for the great acceleration in allegations of negligence. In case you do not know what the contingency fee is, let me say that it is an agreement between the attorney and his client—the plaintiff—in which the attorney agrees to accept a percentage of the damages (money), if such are awarded, as his legal fee. In many instances the attorney's share is 70%, whereas the damaged plaintiff receives but 30%. This type of fee system, we might observe, is not so much the poor man's key to the courthouse as it is the lawyer's key to the bank.

Moreover, this particular arrangement, in respect to the source of the legal fee, is illegal in every country except the United States. Our leaders in Washington blandly discuss their multibillion-dollar projects for improving the nation's health and just as blandly ignore this vicious and immoral contingency-fee system as it operates to the detriment of good medical practice. I think it should be abolished, made illegal, and I think our concerned consumers should be asked to participate to the extent of helping to formulate legislation to outlaw the contingency fee, because in the long run the consumer-patient has to pay for the physician's high premium for malpractice insurance.

Feelings on Fees

I also feel that physicians should have an advance understanding with their patients as to

what fee will be charged and what it will cover and not cover. I also feel that physicians should use discretion in efforts to collect from slow-paying or dissatisfied customers. That is, I think practitioners should exercise prudence before they turn over unpaid accounts to collection agencies or to attorneys for collection. Most collcetion agencies use the contingency-fee system, meaning that they take a percentage of the monies collected as their pay, and as a result they do much coercion and resort to threats to collcet a bill. This sort of thing alienates the patient, who spreads his complaints by word of mouth, and often such a situation is the spark that starts a malpractice suit.

Professional Liability

At present the American Medical Association is in the process of developing a professional liability program in cooperation with the state medical societies and various insurance carriers. Concurrently, the American Medical Association is developing a data center to provide a single repository of informational profiles useful in identifying incidents and causes of liability claims.

Both of these sound like laudable projects.

Medical-Social Evolution

On the brighter side, some things have happened in the past year in the medical-social evolution which deserve comment.

Student Activism

I, for one, am delighted with medical-student activism in organized medicine. I hope it continues and expands, but many of the activists, unfortunately, even as their elders, feel too harassed by other demands on their time to enter into productive participation. Youth tends to have a glorious idealism and confidence that it can put the world right, blissfully unaware that most preceding generations were imbued with similar feelings. Youth is thus inclined to feel that imperfection is caused by the "establishment" rather than that it persists despite efforts of the "establishment" to correct its failings.

Group Practice

I feel very strongly that the increasing tendency toward group practice is all for the good in providing medical care to needy areas. I am not advocating a Kaiser Permanente plan, although it might be good for some areas; on the contrary, freedom of choice of medical group or physician is important and any plan for prepaid care should be evolutionary rather than revolutionary. Fifty-two percent of Minnesota practicing physicians in 1969 belonged to a group of three or more practitioners compared to 41% in 1967. The national average in 1967 was 14%. Parallel to this same vein of thought, I feel that many small towns crying for a physician really do not need one. Transportation, even in respect to vital services, is far different from that of 25 or 30 years ago, when a village medical practice was relatively static because of the imposition of natural physical impediments.

Public Duty

I believe that the Emergency Health Personnel Act, signed into law in 1970, allows Public Health Service physicians, in lieu of the customary two years of military duty, to dispense medical care in areas in which local officials request their presence. This program will be administered by the Department of Health, Education, and Welfare, and although it is not completely new, it will be interesting to see how it operates in some of the ghetto areas which have only one physician for every 10,000 residents.

Catastrophic Health Insurance

I think the inevitable legislation of some type of government-sponsored catastrophic health insurance, similar to that envisaged in the resolution introduced by Dr. Jack Falls and passed by this House of Delegates in 1970 is all for the good.

Women

I think the trend toward more women's and minority groups' being accepted by our medical schools is all for the good. At the end of 1970 there were 334,044 physicians in the United States, a gain of 9,102 over 1969. Of these,

278,535 were engaged in patient-care activities as compared to 261,722 the year before.

Consumer Rights

I think the notion of involving the consumer —the layman—in our Blue Cross plans to let them know why hospitals and medicine are so costly and to share the abusive brunt, is a good one. Blue Cross and other hospital insurance companies are aware of the overemphasis on payment for inpatient care which has resulted in increased use of the most expensive element of health care: the hospital. I believe the policy of Blue Shield plans for adequate public-consumer representation is commendable. In at least eight states the public in such an arrangement is represented by a majority and the physicians by a minority on the corporate body.

Monitoring

The whole area of monitoring not only the quality and quantity and the cost factors of health care—call it "peer review," "medical foundations," or what you will—is inevitably important. I think a responsible profession must take very seriously the allegations that medical care is becoming too expensive. I think we have to establish fair and reasonable fees that are consistent and comprehensive and then demand fairness and honesty on the part of participating physicians. I think I am quoting your incoming President, Bob Kelly, correctly when he said at a meeting of the Medical Services Committee "that we physicians have to set usual, customary and prevailing fees for a given period of time to satisfy the consumer and the insurance carrier." I heartily agree. Then the gougers and defrauders, and there are some, can be dealt with sternly and forcefully.

Rights, Not Privilege

I feel that health care for all is a right and not a privilege. For many of us, re-education in apposition to such newer concepts will be needed and for many the experience will be painful.

Family Physicians

The era which we are now entering, with maximal emphasis on the objective of changing the training of the traditional family physician so that a new type of highly competent, comprehensive, primary-care physician will be produced in sufficient numbers effectively to deliver health care to the American public, is interesting and challenging. But medicine as a whole should not be led by its anxieties into increasing the number of physicians by lowering the quality of their training.

Final Plea

One final plea. In the days ahead, we in organized medicine are going to have to take one of two roads. We can take a militant, strong-union, resort-to-strike plan, as practitioners did in Canada, or we can follow the more democratic plan of negotiating through our leaders with the federal government, and soliciting the understanding of the public, in the hopes of shaping our destinies into acceptable channels. I am for the latter plan.

If ever medicine needs a united front through its county, state and national organizations, it is during these next two years. Each of us must be a battler for the right.

'Tis written in the Hebrew Chronicle,
How the physicians, leaving pill and potion,
Prescribed, by way of blister, a young belle,
When old King David's blood grew dull in motion,
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*Lord Byron: Don Juan, Canto I, Verse CLXVIII 1819.

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Continued on page 490







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Classified Advertisements

(Continued from page 487)

UNIQUE CHALLENGE—THE FAMILY PRACTICE DEPARTMENT of St. Paul-Ramsey Hospital needs an experienced general practitioner. If you want to promote the concepts of general practice and participate actively in the Family Medicine movement, this is for you. This program enjoys the cooperation of all 19 departments at St. Paul-Ramsey and its 50 full-time specialists. It has solid funding and represents a unique blend of patient-oriented care, university academic affiliation and social involvement. For further details regarding academic appointments, salaries and fringe benefits, please contact Vincent R. Hunt, M.D., Director, Department of Family Medicine and Community Health, St. Raul-Ramsey Hospital, St. Paul, Minnesota 55101. Telephone: (612) 222-4260, Ext. 616.

FAMILY PRACTITIONER for an eight man Family Practice group. High earning potential, young active group, expanding into "New Town" suburban community. Opportunity to teach students and Family Practice residents. Robert E. Bundt, M.D., 3809-42nd Avenue South, Minneapolis, Minnesota 55406 (612) 721-6261.

EAST SIDE-ST. PAUL: Doctor's suite available July 1, 1972. Reception room, private office, laboratory, three examining rooms, storage and good parking space. Present Doctor occupant entering teaching field. For information, contact R. H. Rockholt, 1489 Clayridge Avenue, St. Paul, Minn. 55119; Phone (612) 777-7248.

WANTED: Internist or General Practitioner to join Incorporated 5 man group of 4 GPS, and a General Surgeon. 65 bed hospital with ICCU located 65 miles north of Mpls. Good recreational facilities available. For further information contact L. J. Brettingen, M.D. (612) 679-1313.

STUDENT HEALTH PERSONNEL WANTED: Medical Director of Student Health Service, Bemidji State College, Bemidji, Minnesota, 56601. Responsible for programs and health care for 4,700 students. Position available July 1, 1972, or earlier. Contact Dr. C. J. Kemper, Vice President for Student Affairs, Bemidji State College, Bemidji, Minnesota, 56601. Phone: (218) 755-2019.

TWO VACANCIES IN JUNE: Psychiatrist and Internist or General Medicine. Active outpatient clinic, Winston-Salem. Normally 40-hour workweek. Excellent facilities, retirement and insurance plans; liberal vacation and sick leave benefits. Can pay moving expenses. Salary range $23,424-$29,-848. Any state or DC license required. Equal opp. employer. Write Chief of Staff, VA Hospital, Salisbury, N.C. 28144.

HIGHLAND PARK OFFICE SPACE at $6.00 per square foot. All utilities furnished. Zoned heating and air conditioning, carpeted. New Highland Professional Bldg. 621 So. Cleveland Avenue, St. Paul. Dr. Jack Shepard 699-1709.

PSYCHIARIST-CHALLENGING OPPORTUNITY TO practice progressive and innovative treatment to wide variety of mental disorders; excellent facilities and ancillary staff; comfort of small town living with nearby city conveniences; excellent school system; good climate; regular hours, 30-day vacation, exc. retirement, life, health ins. plans; can pay moving expenses; salary range $23,424-$29,848; any state or DC license required; equal opp. employer. Write Chief of Staff, VA Hospital, Salisbury, N.C. 28144.

SPOONER-WASHBURN COUNTY: Needs a surgeon. An opportunity to live in one of the more beautiful spots in the country surrounded by wilderness areas with unending lakes and streams. A fine school system away from urban crises, and still within easy driving distance from St. Paul-Minneapolis. A rewarding varied medical experience financially competitive with any other area. Contact Rudy Matzke, M.D., Spooner Clinic Ltd, Spooner, Wisconsin 54801. Phone (715) 635-2151.

GENERAL PRACTITIONER: County seat community of 2000. Modern 35 bed hospital 4 blocks from fully equipped clinic. Present associate retiring January 1, 1973. Early partnership. Contact H. A. Knoche, M.D., Gaylord, Minnesota 55334. Telephone 612-237-2528.

Minnesota State Medical Association

It's All Set for You in '72

119th Annual Meeting

Mini-scientific sessions, maxi-scientific sessions, exhibits, luncheons, banquets, House of Delegates and reference committee meetings are some of the events which promise to insure that the 119th Annual Meeting of the MSMA, May 18 through 20, in Rochester will remain true to its reputation as the Upper Midwest's Great Medical Meeting.

A unique feature will be an open hearing for physicians conducted by the American Medical Association in conjunction with this year's Annual Meeting.

The AMA Council on Long Range Planning and Development has selected Minnesota as one of only two states for these hearings to be held prior to comparable hearings planned for the AMA's Annual Convention June 18-22 in San Francisco.

The Minnesota hearings will be divided into two sessions, the first to be held from 2 to 5 P.M. on Thursday, May 18, and from 9 to 12 Noon on Friday, May 19. The purpose will be to give physicians in the area an opportunity to speak their minds on AMA policies and procedures. Following are the general subjects chosen for discussion: 1. Proposed changes in the AMA constitution and By-laws, 2. Organization structure, and 3. Delineation of committee responsibilities. Physicians who wish to appear as witnesses have been previously requested to submit their statements to the AMA by May 5.

University of Minnesota president Doctor Malcolm Moos will be the Thursday Annual Meeting luncheon speaker. The Friday luncheon speaker will be Doctor Charles C. Edwards, Commissioner of the Food and Drug Administration, Department of Health, Education and Welfare.

Included in the schedule of afternoon "in depth" maxi-sessions on Thursday will be a double session (2:00-5:00 P.M.) titled "Recognition and Management of the Dependent Person," sponsored by the Committee on Mental Health, Subcommittee on Alcoholism and Drug Abuse. The MSMA Committee on Environmental Health will also sponsor a two part session on Friday (2:00-5.00 P.M.) titled "Patient Care and Pollution Problems." This symposium is open to physicians, nurses and hospital administrators.

Seven of this year's scientific sessions have been arranged by the Minnesota Chapter of the American College of Surgeons.

Physicians attending the Annual Meeting will have the opportunity to "meet your medical school deans" at one of the Thursday afternoon sessions. Present will be associate deans from the University of Minnesota Medical School, the Mayo Graduate Medical School and the dean of the new U of Minnesota Medical School, Duluth.

A detailed schedule of additional scientific sessions follows this Annual Meeting preview.

Tee-off time for the annual Physicians' Golf Tournament is Wednesday, May 17, 2:00 P.M. at the Rochester Golf and Country Club. Prior to the tournament a 12:30 P.M. stag luncheon will be served. The registration fee of $10.00 includes luncheon and tournament green fees.

Tennis tournament—Men's Singles Wednesday, May 17, 2:00 P.M., at the Rochester Tennis Club. Entry Fee, $3.00—pre-registration requested. Payment at the Tennis Club. Doubles upon request. Contact: Dr. Clark Millikan, Mayo Clinic.

The Annual Banquet is scheduled for Thursday, May 18, 7:00 P.M. It will be preceded by the President's Reception at 6:00 P.M.

The House of Delegates will convene for its opening session Wednesday, May 17, 1:00 P.M., and reference committees will meet at 4:00 P.M. and 7:30 P.M. following the close of the first session of the House. The second session of the House of Delegates will meet Friday at 2:00 P.M.

The Committee on Scientific Assembly is pleased to announce the following special events scheduled by specialty societies in conjunction with the Annual Meeting:

The Minnesota Physiatric Society will hold a dinner meeting Friday, May 19.

The Minnesota Chapter of the American College of Surgeons will hold a luncheon on Friday, May 19, 12:15 with a business meeting following.

The Minnesota Academy of Ophthalmology and Otolaryngology will hold a cocktail hour and dinner Friday, 6:30 P.M., Council Meeting preceding at 5:00 P.M.

A spring all-day meeting of the Minnesota Society of Clinical Pathologists, beginning at 9:00 A.M., Saturday, May 20.

A luncheon meeting, Minnesota Chapter of the Flying Physicians Association Saturday, May 20, 12:00. Interested physicians are urged to contact Alex Webb, Jr. M.D., 311 Terminal Bldg., Minneapolis-St. Paul International Airport, Mpls. or Frank J. Bonello, M.D., 1074 So. Robert St., West St. Paul.

Physicians are encouraged to save time by preregistering. Pre-registration materials are enclosed with all Annual Meeting mailings.

Take Time Out for these Special Events

Sessions Run Concurrently

Wednesday, May 17

GOLF TOURNAMENT — Luncheon and tournament
Stag Luncheon —
12:30 P.M. — Rochester Golf and Country Club
Tee-off —
2:00 P.M. — Rochester Golf and Country Club
Registration Fee —
$10.00 (includes luncheon & tournament greens fee)
Caddies, carts available, but not required
Open bar following tournament— prizes and trophies awarded
Reservations requested
(Dr. Frederick D. Banfield, Rochester, Chairman of Golf Committee)

1:00 P.M. —
House of Delegates 1st session — Kahler Hotel

4:00 P.M. —
Reference Committees Meet — Kahler Hotel

6:00 P.M. —
Delegates and Councilors Dinner — Kahler Hotel

8:00 P.M. —
Reference Committees Reconvene

Thursday, May 18

7:30 A.M. —
Committee breakfast meetings

8:00 A.M. —
Registration — Mayo Civic Auditorium

12:15 P.M. —
Annual Meeting Luncheon — Kahler Hotel
Speaker: President Malcolm Moos, University of Minnesota

4:00 P.M. —
MINNPAC Membership Meeting — Regency Room, Kahler Hotel

6:00 P.M. —
President's Reception — Kahler Hotel

7:00 P.M. —
Annual Banquet — Kahler Hotel

Friday, May 19

7:30 A.M. —
Committee breakfast meetings

12:15 P.M. —
Annual Meeting Luncheon, Kahler Hotel
Speaker: Dr. Charles C. Edwards, Commissioner of Food and Drugs, Department of Health, Education and Welfare, Food and Drug Administration

12:15 P.M. —
Luncheon and Meeting — **Minnesota Chapter, American College of Surgeons** — Windsor I, Kahler Hotel

2:00 P.M. —
House of Delegates, 2nd Session

6:00 P.M.
Dinner Meeting, **Minnesota Physiatric Society** — Centennial Room, Kahler Hotel

6:30 P.M. —
Cocktails and Dinner — **Minnesota Academy of Ophthalmology & Otolaryngology,** Holiday Inn Downtown

Friday, May 19

8:00 P.M. —
H. M. S. Pinafore, by Rochester Civic Theater
Tickets: $3.50

Saturday, May 20

9:00 A.M. —
Meeting of **Minnesota Society of Clinical Pathologists,** Mann Hall, Mayo Clinic Medical Sciences Building

12:00 P.M.
Luncheon and reconvened meeting, **Minnesota Society of Clinical Pathologists,** Mann Hall, Mayo Clinic Medical Sciences Building

12:00 P.M. —
Luncheon Meeting, **Minnesota Chapter of the Flying Physicians Association,** Gold Room of Holiday Inn Downtown
$4.25 reservations requested

Mini-Scientific Sessions

Thursday, May 18

9:00 A.M.

Laparoscopy
J. E. Wall
Vesicoureteral Reflux
P. P. Kelalis
Exercise-Coronary Heart Disease
J. I. Thompson

9:20 A.M.

Surgical Emergencies — Newborn
B. J. Spencer
Emergency Care — Accident to Hospital
C. R. Hitchcock
Polychemotherapy, Lymphoma
I. J. Lerner

9:40 A.M.

Fetal Monitoring
D. L. Hill
Coronary Artery Surgery
D. M. Nicoloff
Use of L-Dopa
L. A. Farber

10:00 A.M.

Hyperbilirubinemia, Newborn
C. W. Jarvis
Hemorrhoids: Surgery vs No Surgery
W. T. Smith
Can Gallstones be Dissolved?
J. L. Thistle

10:15 A.M.
Recess To View Exhibits

10:45 A.M.

Occular Complications
D. M. Robertson
Surgical Treatment, Thyroid Nodules
O. H. Beahrs
Ambulatory Emphysema
F. M. MacDonald

11:05 A.M.

Malignant Melanoma
J. C. Ivins
Diffuse Pulmonary Disease — Transbronchial Lung Biopsy
H. A. Andersen
Treatment of Gout
R. S. Colton

Thursday, May 18

11:25 A.M.

Management of Asthma
J. P. Lillehei
Surgical Treatment, Early Lung Cancer
J. Fuller
Urinary Tract Infection in Women
L. H. Smith, Jr.

11:45 A.M.

Upper Airway Problems — Anesthesia
J. J. Buckley
Asymptomatic Cholelithiasis
E. S. Judd
Irritable Colon Syndrome
W. D. Blackwood

Friday, May 19

9:00 A.M.

New Antibiotics
R. P. Gruninger
Gonorrhea — Current Treatment
A. L. Schroeter
*New Methods — Pain Control
D. M. Long

9:20 A.M.

TB Chemotherapy
D. T. Carr
Borderline Hypo & Hyperthyroidism
A. L. Schultz
*Plastic Surgery: Snowmobile Injuries
C. I. Karleen

9:40 A.M.

Urinary Tract Infection — Children
W. J. Brooker
Radiation Therapy in Cancer
S. H. Levitt
*Trauma to Larynx
Barclay Cram

10:00 A.M.

Renal Masses — Urographic Techniques
E. E. Fraley
*Hyperalimentation, Intravenous
R. L. Telander
Alternate Day Corticosteroid Treatment
R. G. VanDellen

10:15 A.M.

Recess To View Exhibits

10:45 A.M.

Diagnosis, Treatment, Nocturnal Enuresis
D. C. Merrill
Serum Multiple Analysis Patterns, Diagnosis
R. L. Reece
*Vaginal Hysterectomy in Younger Women
T. J. Williams

11:05 A.M.

"Brittle" Juvenile Diabetics — the Somogyi Effect
H. S. Sauls
Hyperlipidemia
J. L. Juergens
*Bile Acid Metabolism: Surgical Significance
A. F. Hofmann

11:25 A.M.

Current Concepts — Osteoporosis
D. L. Hoffman
Hypertension
L. A. Tobian
*Total Hip, and Other Joint Replacement
M. B. Conventry

11:45 A.M.

Cutaneous Clues, Systemic Malignancy
H. O. Perry
"Bleeders"
W. R. Swaim

*Arranged by Minnesota Chapter of the American College of Surgeons.

Afternoon In-Depth Maxi-Scientific Sessions

Thursday, May 18

2:00 P.M.

Recognition, Management — The Dependent Person (2:00-5:00 P.M.)
Subc. Alcoholism, Drug Abuse, Committee Mental Health
Dumping Syndrome
M. A. Adson, Chm.
Arrhythmias, Blocks, Pacemakers
Yang Wang, Chm.
Meet the Medical School Deans
R. D. Miller, Chm.
Transient Cerebral-Ischemic Attacks
C. H. Millikan, Chm.

3:00 P.M.

Recess To View Exhibits

3:45 P.M.

Biliary Tract Problems
D. C. McIlrath, Chm.
Hepatitis Associated (Australia) Antigen
J. McCullough, Chm.
Psychiatric Aspects of Pain
M. J. Martin, Chm.
Mesenteric Vascular Disease
O. W. Kincaid, Chm.

Friday, May 19

2:00 P.M.

Environmental Health (2:00-5:00 P.M.)
Comm. Environmental Health
Oral Hypoglycemic Agents
F. C. Goetz, Chm.
Massively Injured Patient
J. F. Perry, Jr., Chm.
Epilepsy in Children
R. V. Groover, Chm.
Ovary Carcinoma
K. A. Prem, Chm.

3:00 P.M.

Recess To View Exhibits

3:45 P.M.

Patient with Ischemic Extremity
J. R. Pluth, Chm.
The Family Physician — Most Important Link, — Early Identification — Vision, Hearing Problems
Minn. Academy of O. & O.
Care & Management, Cerebral Palsied — — New Concept
United Cerebral Palsy of Minnesota
Medical Audit
J. M. Schless, Chm.

Mini and Maxi-Scientific Sessions held in Mayo Civic Auditorium and Art Center.

Meeting

Northlands Regional Chapter of the American College of Chest Physicians

The annual meeting of the society is planned for May 6th, 1972, at Mann Hall, Medical Science Building, Mayo Clinic, Rochester, Minnesota.

Theme of the morning meeting will be "Chronic Obstructive Lung Disease" and of the afternoon meeting "Coronary Artery Disease."

Help put our best natural resources to work.



As you know, today there is a crying need for technicians.

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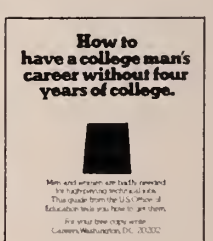
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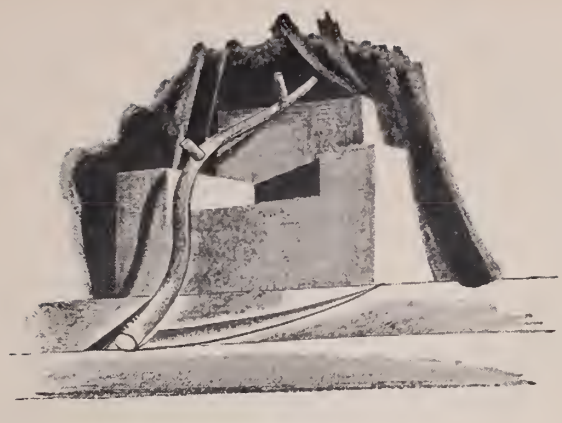
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In Memoriam

I have trodden the winepress alone.—Isaiah. LXIII. 3

ROY A. LUNDBLAD, M.D.

Dr. Roy A. Lundblad, 66, died March 30 in Oceanside, California. A 1929 graduate of the University of Minnesota Medical School, he had been in practice for 37 years until his retirement in 1966. He was named chief of staff at Swedish Hospital, now Metropolitan Medical Center, in 1957, and had served in the Army Medical Corps. in World War II.

Dr. Lundblad was a member of the Hennepin County Medical Society and the American Medical Association, and an Associate Member of the Minnesota State Medical Association.

He is survived by his wife, Evelyn, a son, Rodger, and a daughter, Karen.

GEORGE A. EARL, M.D.

Dr. George A. Earl, 87, surgeon, died March 17. Dr. Earl served as President of the Minnesota State Medical Association in 1939, was a Council member from the Fifth District from 1933 to 1938, and for the years 1935 to 1938, served as Chairman. He also was a long-time Chairman of the Committee on Medical Economics which formerly served as a connecting link for many important economic and social committees of the State Association.

In addition, Dr. Earl was one of the organizers of the Medical Alumni Association of the University of Minnesota, served as secretary of the Mayo Memorial Medical Commission for the erection of the Mayo Medical Building on the University campus, and was a co-founder of the Association of Baptist Homes and Hospitals. He was also a member of the American Medical Association and Ramsey County Medical Society and a Life Member of the Minnesota State Medical Association.

He is survived by his son, Roland, and a daughter; Mrs. Edward P. Davis.

OSCAR J. ENGSTRAND, M.D.

Dr. Oscar J. Engstrand, 76, Minneapolis surgeon for 50 years, died January 14, after a long illness. He had an office in the Physicians and Surgeons Building up to five years ago and had been on the Swedish Hospital staff for 40 years.

He was born in Dawson, Minnesota, and was a member of the Hennepin County Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

Dr. Engstrand is survived by his wife, Florence, and three daughters, Elizabeth, Audrey and Jacquelyn.

THOMAS M. GRIFFIN, M.D.

Dr. Thomas M. Griffin, 41, anesthesiologist at St. Lukes Hospital, St. Paul, died March 24. He was born in Kildysart, County Clare, Ireland, and had lived in Mendota Heights for 12 years.

He was a member of the American Medical Association, Ramsey County Medical Society, the Minnesota State Medical Association, the American Society of Anesthesiologists, a graduate of the Royal College of Surgeons and Physicians of Dublin and had done postgraduate work at the University of Minnesota.

He is survived by his wife, Irene, a daughter, Patricia, and four sons, Thomas, Brian, Cathal and Colm.

ROBERT L. WILDER, M.D.

Dr. Robert L. Wilder, 71, a longtime Minneapolis pediatrician, died February 25, in San Miguel, Mexico.

A University of Minnesota graduate, Dr. Wilder practiced medicine from 1926 until 1957, when he retired. He was an associate clinical professor of pediatrics at the University and in 1947 was chief of staff at Abbott Hospital. Dr. Wilder was a member of the Hennepin County Medical Society, the American Medical Association, a Fellow of the American Academy of Pediatrics, a member of the American Forestry Association, the American Physicians Art Association, the Minnesota Society of Sculptors and an Associate Member of the Minnesota State Medical Association.

The March issue of MINNESOTA MEDICINE carries one of Dr. Wilder's paintings "Mexican Pilgrimage."

Dr. Wilder is survived by his wife, Alfreda, sons, Dr. Walter L. Wilder of Minneapolis, and John, and a daughter, Martha.

VICTOR H. GARDNER, M.D.

Dr. Victor H. Gardner, 78, founder of the Fairmont Community Hospital, Fairmont, died March 9. A graduate of Leander Clark College, Iowa City, Iowa, Dr. Gardner received his medical degree from the University of Iowa Medical School. He interned in obstetrics and gynecology at the University of Iowa Hospital and practiced in Estherville, Iowa, before moving to Fairmont.

He was a member of the Blue Earth Valley Medical Society, the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.



A MINNPAC INVITATION

The MINNESOTA MEDICAL POLITICAL ACTION COMMITTEE invites you to support the singularly most effective means available to make medicine's voice heard in the political arena—MINNPAC/AMPAC.

Join MINNPAC today. Participate in the political and governmental process which will ultimately determine how the practice of medicine will be structured during this decade. Your $25.00 includes both MINNPAC and AMPAC dues and will be used to assist in electing responsible men and women in both parties to the State Legislature and to Congress. The MINNPAC Board of Directors is charged with the responsibility of urging physicians and their wives to become actively involved in the support of candidates and the party of their choice. *YOUR* help is needed *NOW!* Complete the application form or merely send your $25.00 check to: MINNPAC, Metro Medical Building, 825 South 8th Street, Room 503, Minneapolis 55404.
P.S. Those of you who have already sent your check—*Thank You!*

☐ Please bill me $25.00 for my annual membership in MINNPAC and AMPAC.
☐ Membership contribution is enclosed.

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"The history of science, and in particular the history of medicine... is... the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

– George Sarton, from "The History of Medicine Versus the History of Art"

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Opinion & Dialogue

Dialog

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

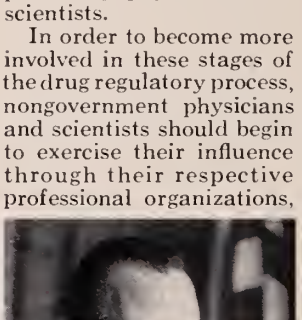
Herbert L. Ley, Jr., M.D., M.P.H., Formerly Commissioner, F.D.A. (1968-1969)
Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations,



state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the puhlic. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of wha the medical community *and* federal regulators d will often be represented i simplistic and somewha misleading terms.

One illustration of th misuse of the media in thi regard is the recall of anti coagulant drugs severa years ago. This FDA actio was given publicity by th press and television tha went far beyond its prob able importance. The resul was a very uncomfortabl situation for the practi tioner who had patient taking these medications Since the practitioner an pharmacist had not bee informed of the action b the time it was publicized in most states they wer deluged with calls fron worried patients.

The practitioner can at tempt to solve these prob lems of inadequate commu nication in several ways One would be the creatio of a communications lin in state pharmacy societies When drug regulation new is to be announced, the so ciety could immediatel distribute a message to ev ery pharmacist in the stat The pharmacist, in turn could notify the physician in his local community s that he and the physicia could be prepared to an swer inquiries from pa tients. Another approac would be to use profes sional publications th practitioner receives.

All of this leads back t my opening contention: drug regulation is to be effective, timely, and relate to the realities of clinic practice, a better method communication and fee back must be developed b tween the nongovernmen tal medical and scientif communities and the regu latory agency.

ue

Maker of Medicine

Henry W. Gadsden, hairman & Chief Executive Officer, Merck & Co., Inc.



In my opinion, it is the sponsibility of all physi- ans and medical scientists take whatever steps they ink are desirable in a law- nd regulation-making ocess that can have far- eaching impact on the actice of medicine. Yet any events in the recent ast indicate that this is t happening. For exam- le, it is apparent from ug efficacy studies that e NAS/NRC panels gave ttle consideration to the idence that could have en provided by practic- g physicians.

There are several current velopments that should crease the concern of acticing physicians about ug regulatory affairs. One the proliferation of mal- actice claims and litiga- on. Another is the effort government to establish e relative efficacy of ugs. This implies that if physician prescribes a ug other than the "estab- shed" drug of choice, he ay be accused of practic- g something less than rst-class medicine. It ould come perilously ose to federal direction of ow medicine should be acticed.

In order to minimize this ind of arbitrary federal ction, a way must be und to give practitioners oth voice and represen- tation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

Opinion & Dialogue

What is your opinion, doctor?
We would welcome your comments.

P·M·A

The Pharmaceutical Manufacturers Association
1155 Fifteenth Street, N.W., Washington, D.C. 20005

Letters to the Editor

Dear Editor:

The history of the development of the metric system around the world is probably of little interest to the average citizen of the U.S. However, the fact that our country will soon be one of only nine nations not using the metric system, should be of great concern to each citizen of the United States.

On July 31, 1971, the Secretary of Commerce presented to the Congress a report titled: "A Metric America—A Decision Whose Time Has Come." This report urges that the country begin a 10 year program to convert completely to the metric system. In 1878 the AMA recommended the use of the metric system in medical practice and research. On November 1, 1971, the *Journal* of the AMA announced that the modified metric system known as SI (System Internationale d'Unites) would be used exclusively in that journal beginning in 1973.

The change to metric will not be painless and will not be accomplished without involving each person in the United States. We in the medical profession, use to the convenience and symplicity of the metric system, and largely converted to metric in our professional lives, can help to make this inevitable change less troublesome.

As a start in making this change, I urge the editorial board to set a date for completion of the change to metric for all medical and scientific measurements published in MINNESOTA MEDICINE. This does not involve much more than height, weight, and body temperature. This change should not be too difficult and should not be delayed unnecessarily.

Charles W. Jarvis, M.D.
St. Paul, Minnesota

Dear Editor:

I have enjoyed browsing through the January issue, as I always do, but I write you to protest that "herniae" (page 33) is very much like the story of the professor who said that his wife had so much laundry to do, that she needed two Bendices. I suggest that "hernia" has become an English word rather than a Latin one, and the plural is "hernias."

Harry L. Arnold, Jr., M.D.
Honolulu, Hawaii

Agree. Herniae are consigned to the classic rooms of Musea. Ed.

Allergic Reactions

I am compiling case reports of allergic reactions to biting insects, i.e., mosquitos, fleas, kissing bugs, bed bugs, gnats and flies—including horsefly, sandfly, deerfly. I am also interested in reactions to fire ants.

I would like physicians to supply me with case reports of those patients who have had reactions to such insects. Include in your reports, the history of the type of reaction and complications if any; the immediate treatment; if desensitization were attempted, what were the results? Send to:

Claude A. Frazier, M.D.
4-C Doctors Park
Asheville, N.C. 28801.

Claude A. Frazier, M.D.

Clinical Path Conference

A Steroid-Induced Infectious Complication of Rheumatoid Arthritis

George Kitzmiller, M.D.:

A 63-year-old man came to General Hospital in January, 1969, because of abdominal pain. Chronic deforming rheumatoid arthritis involving the fingers and ankles had been present since 1960 but controlled by prednisone, 15 mg. daily. Joint examination showed proximal interphalangeal joint hypertrophy; ulnar deviation of the fingers, and a warm, swollen left ankle. There was a mild normochromic, normocytic anemia with a reduced serum iron and iron binding capacity. Lumbar spine xrays showed chronic degenerative arthritis. A film of the left ankle revealed marked narrowing of the ankle mortis. Soft tissue swelling was suggestive of an acute pyogenic or tuberculous arthritis. A barium enema showed sigmoid colon diverticuli; and a clinical diagnosis of diverticulitis was made.

The patient was readmitted in February, 1969, for pre-olecranon bursitis and acute arthritis of the right wrist and left ankle. Cultures of the blood and draining joint sinuses showed penicillin-resistant staphylococci. Prostaphlin, 500 mg., and penicillin, 2,000,000 units, intravenously every six hours resulted in remission of fever and sinus drainage. Intermittent pain and swelling of the left ankle continued after discharge in late March, 1969.

After the admission on May 3, 1969, both preolecranon bursae were drained and the patient was treated with antibiotics. On May 10 he developed left lower quadrant abdominal pain and tenderness which increased on May 12. Subdiaphragmatic air was noted on x-ray. At operation an indurated abscess around the rectosigmoid was found and a collection of pus was present in the cul-de-sac. Penrose drains were placed in the pelvis and both colonic gutters, and sump drainage was inserted in the pouch of Douglas. A right transverse colostomy was performed.

Following surgery there was slow improvement until May 17, 1969, when the patient developed acute pulmonary edema. Subsequent serial electrocardiograms were compatible with an acute non-transmural myocardial infarction. This was treated with digitalis and diuretics, and he again began to improve slowly until May 23, 1969. At this time, intermittent confusion and lethargy were noted. These continued and on May 30, the confusion, incoherence, and hyperactivity became much more pronounced. On June 3, he developed coma and shock. After treatment with isuprel and plasma, urine volume and blood pressure were temporarily restored. Arterial blood Ph was 7.33; PCO 43 mm. of mercury; and PO2 67 mm. of mercury. The coma continued, shock recurred, and the patient died eight hours later. Accompanying Tables 1 through 4 detail the laboratory data, culture reports, and antibiotic and steroid therapy.

TABLE 1
Antibiotic Therapy

1. Penicillin 2,000,000 units Prostaphlin 500 mg. Q-6-h. I.V.	5/ 3 - 5/10
2. Penicillin 2,000,000 units Prostaphlin 500 mg. Tetracycline 500 mg. Gantrisin 500 mg. Q-6-h. I.V.	5/10 - 5/11
3. Gantrisin 500 mg. Q-6-h. I.V.	5/11 - 5/13
4. Keflin 1.0 gm. Q-4-h. Q-4-h. I.V.	
Kantrex 150 mg. Q-8-h. I.M.	5/13 - 5/27
Colymycin 150 mg. Q-12-h. I.M.	5/23 - 5/25
5. Colymycin 50 mg. Q-8-h. I.M.	5/28 - 6/ 2
Keflin 1.0 gm. Q-6-h. I.V.	5/28 - 6/ 1
Kantrex 250 mg. Q-12-h. I.M.	5/30 - 6/ 1
6. Keflin 3.0 gm. Q-6-h. I.V.	6/ 2 - 6/ 3

TABLE 2
Steroid Therapy

1. Prednisone 15 mg/day (o).	5/ 3 - 5/10
	5/27 - 6/B
2. Solu-Cortef 50 mg/day (I.M.)	5/13 - 5/26

TABLE 3

DATE	SOURCE	ORGANISM	SENSITIVITY 1	2	3	4	5	6	7	8	9	10	11	12
5/ 3	Rt. elbow	Staphylococcus		S	S	S		S	R	S	S			
		Anaerobic streptococci												
	Sputum	Mixture, N.P.O.*												
5/ 7	Rt. elbow	Staphylococcus		S	S	S		S	R	S	S			
5/ 7	Urine	Negative												
5/10	Urine	20,000 colonies yeast												
5/11	Urine	Negative												
5/12	Peritoneal fluid	E. coli	R	S	S	S	S	S						
		Proteus	S	S	R	S	R	R	R			R	R	R
		Alpha streptococci												
		Anaerobic gram positive rods resembling cl. perfringens												
5/19	Urine	Negative												
	Sputum	Escheriachia (paracolon intermedia)	S	S	S	S	S	S	R			R	S	R
	Sump Drainge	Pseudomonas												
5/24	Urine	2000 colonies pseudomonas												
5/28	Urine	Negative												
5/29	Sputum	Mixture, N.P.O.*												
	Urine	Negative												
5/30	Abdominal drain	E. coli	S	R	R	R	S	R				R	S	S
		Klebsiella	R	R	R	R	S	R				R	S	R
		Alpha streptococci												
		Anaerobic gram positive rods												

1 Streptomycin 4 Kantrex 7 Penicillin 10 Polycillin
2 Tetracyline 5 Colymycin 8 Lincocin 11 Furadantin
3 Chloromycetin 6 Keflin 9 Prostaphlin 12 Gantrisin
*N.P.O.—No predominant organism

TABLE 4

DATE	T°F	WBC	%PMN	BUN	NA+	K+	WT#
5- 3	101	8,100	93		135	4.7	
5- 4	101						
5- 5	100	12,700	94	6	128	4.0	
5- 6	100						
5- 7	99	7,300	79				
5- 8	99						
5- 9	99	10,800	86				
5-10	100.6	23,000	94				
5-11	100.8	24,800	96		140	4.0	108
5-12	101.6	16,900	94	5	127	4.0	104
5-13	101	16,200	95	7	122	3.3	106
5-14	100	14,100		4	123	3.7	107
5-15	99.6	15,100		2	123	4.0	109
5-16	101.4	15,100		3	123	3.8	107
5-17	101.4			4	126	3.8	106
5-18	101.6	15,300		6	131	4.0	101
5-19	101.4	12,400		6	133	3.9	102
5-20	99.8	9,800		6	137	3.9	103
5-21	99.2	-		5	137	4.1	100
5-22	99.6	11,600		6	135	4.2	98
5-23	100.6	10,700		5	138	4.5	97
5-24	99.4	14,600		5	134	5.1	96
5-25	100						93
5-26	99.2	10,400	93	9	143	3.4	91
5.27	100.4						93
5-28	101	11,400	82		140	3.2	91
5-29	102						92
5-30	102.6	14,100			134	4.1	9.1
5-31	102.4	13,900	81				92
6- 1	102.8				135	4.9	94
6- 2	102	23,900	93	18	130	4.3	90
6- 3	97	26,300		27	128	3.9	92

Clinical Discussion

Russell Payson, M.D.:

In evaluating this very complex history it should be noted that the patient had suffered from rheumatoid arthritis since 1960. A dosage of prednisone was maintained until his final illness without interruption. In January, 1969, he was seen here with abdominal pain and active joint disease. We are not told what happened to the ankle joint. I assume the non-operative management of the diverticulitis included antibiotics; so perhaps there was improvement.

Signs of acute septic arthritis recurred in February, 1969, and penicillin resistant staphylococci were cultured from the blood and draining sinuses. The patient was treated with Prostaphlin and intravenous penicillin with some improvement; however, intermittent joint symptoms persisted. Joint symptoms and drainage recurred three weeks prior to his final admission in May, 1969. Bowel perforation, pelvic abscess, acute pulmonary edema, and myocardial damage further complicated his clinical course. He appeared to improve on congestive heart failure medication but became confused and disoriented. Signs of mental confusion, incoherence, and lethargy persisted until death.

X-ray Discussion

Oscar Lipschultz, M.D.:

Xrays (Figure 1) of the left ankle in January 1969, revealed arthritis of the left ankle, which does not have the appearance of a rheumatoid or degenerative kind but is characteristic of an infectious type of arthritis. Soft tissue swelling and loss of joint space is present. An xray of the right elbow shows soft tissue swelling characteristic of a pre-olecranon bursitis.

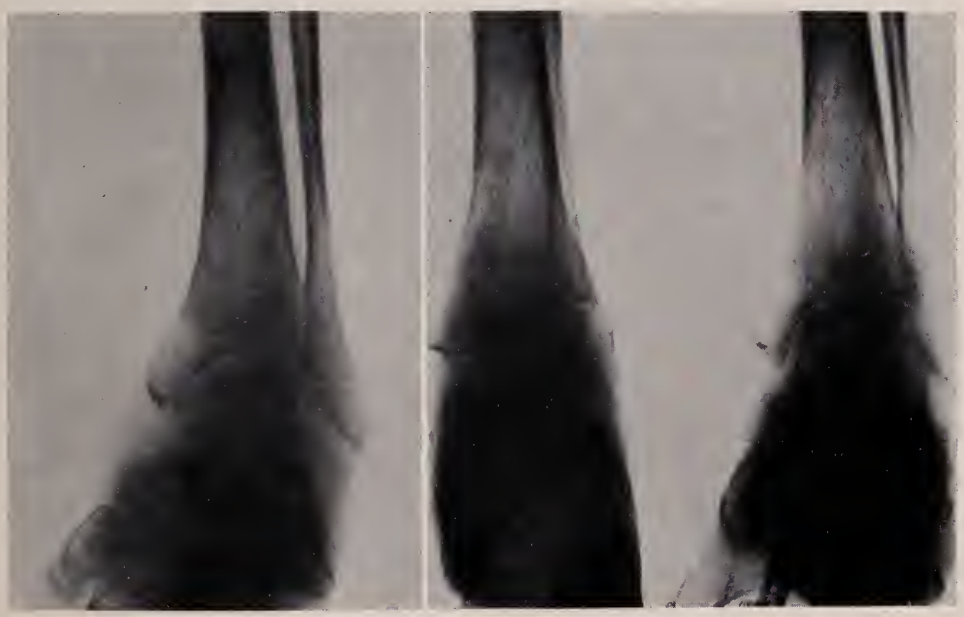


Fig. 1—Roentgenogram of ankle suggestive of septic arthritis.

A series of abdominal films also taken in January are suggestive of small or large bowel obstruction. A barium enema study on Janaury 19 confirmed the presence of sigmoid diverticulosis with associated acute diverticulitis.

We can use this film to show the lumbar spine which suggests an old fracture of the lumbar vertebra but does not suggest metastases or old rheumatoid spondylitis. We can also note a large distended bladder indicating paralysis of the bladder or improper emptying due to obstruction at the level of the prostate.

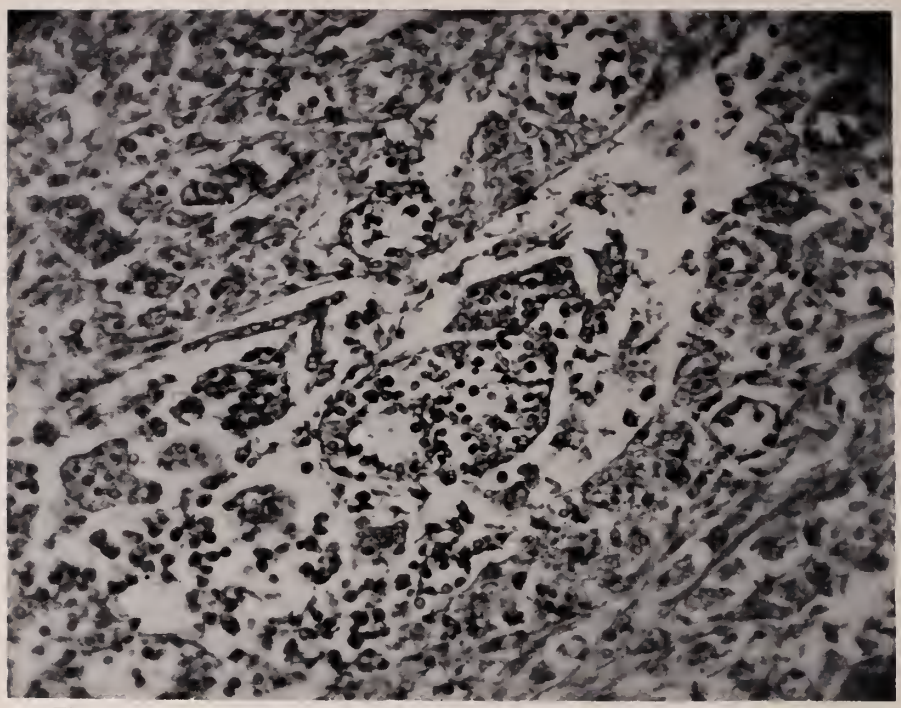


Fig. 2-X400 Prostate showing budding organisms of cryptococcus neoformans.

The admission chest x-ray on May 3, revealed a relatively normal chest with normal heart size. An abdominal film, taken on May 11 shows air under the left diaphragm. I assume that this film was taken just prior to surgery and was probably the basis for a diagnosis of rupture of an air-containing viscus.

On May 18 the patient developed a beautiful example of pulmonary edema with a typical butterfly appearance but without enlargement of the heart. One must also consider the possibility of an active bronchopneumonia at this time. Thereafter, the pulmonary roentgenographic studies progressively improved until near the time of death when there remained only a residual consolidation of the lower lobe.

In summary, the patient had an arthritis about the left ankle of an infectious type with abundant destruction; a pre-olecranon bursitis of the elbow, and pulmonary edema which improved most markedly on the final admission, leaving only a residual consolidation of the left lower lobe of the lung.

Discussion

Dr. Payson:

This is the first CPC I have ever seen in which the diagnoses listed in the protocol satisfactorily explain all the data. You can look at this man as a rheumatoid arthritis patient who developed multiple pyarthroses of the right wrist and the left ankle, followed by pre-olecranon bursitis, a common phenomenon in rheumatoid arthritis. The pre-olecranon bursitis is usually due to staphylococci which enter a break in the skin or mucosa, become a bacteremia, and settle in an area of inflammation about a joint. This is a particularly common phenomenon in patients with rheumatoid arthritis, especially those who have been treated with steroid therapy.

This patient also appears to have had well documented diverticulitis. He had a complicated course during his last admission, culminating in bowel perforation with pelvic abscess and surgery. Thereafter, he developed congestive heart failure and signs of a myocardial infarction. Further, he became disoriented, a fact not thoroughly explained in the protocol; but then he was anoxic and had congestive

heart failure. So there is really not much in the protocol that is not explained by the course of clinical events. It wouldn't be a challenge to stick with the diagnoses given to me; so I am going to discuss some other possibilities.

Differential Diagnoses

Rheumatoid Arteritis

The first diagnoses one might consider is rheumatoid arteritis, an entity which offers a good explanation for some of the events in the protocol. Rheumatoid arteritis is a phenomenon that occurs in association with rheumatoid arthritis, particularly in these patients who are treated with steroid medication. It most often occurs in older patients and is seen to closely mimic *periarteritis nodosa.* It may involve the bowel and cause infarcts, and it would be very difficult to *distinguish such bowel infarctions from acute diverticulitis.* It can also involve the coronary arteries and cause heart attacks; hence this would be a convenient link to tie things together in one package. It can also be associated with cerebral arteritis and lead to disorientation, confusion, and stroke symptoms.

Against this diagnosis is the absence of evidence of involvement of the skin or the nerves. There usually is some evidence of a neuritis or a neuropathy, which is not observed in this case. Areas of gangrene, particularly of the extremities, are quite common with rheumatoid arteritis, and these are not reported in this case. Gangrene of the extremities is encountered more commonly in rheumatoid arteritis than in periarteritis nodosa. The white count is usually not quite as high as was observed in our patient, but can go quite high. In view of the fact that we have staphylococci in the blood and in the joint fluid, I am disinclined to make a diagnosis that is not primarily infectious in origin.

Bacterial Endocarditis

I asked myself whether this man could have infective bacterial endocarditis: a favorite CPC diagnosis, particularly to a physician interested in infectious diseases. Infective endocarditis could explain a couple of the events in the clinical course. For instance, he could have had a coronary embolism to account for his episode of coronary thrombosis. Infective emboli could explain the infarction of the bowel with pelvic abscess and other evidence of embolic phenomena, particularly to the nervous system. However, he never developed red cells in his urine or splenomegaly, both of which may be expected with prolonged subacute bacterial endocarditis. The hemoglobin also remained remarkably stable, if one wishes to invoke the diagnosis of infective endocarditis. Most individuals with infective endocarditis show a prominent fall in the hemoglobin level. In addition, his blood urea nitrogen remained quite low until terminally.

Pyemia

I think what this man actually had is an old-fashioned disease which I call pyemia. We really don't encounter pyemia too frequently these days, but it is occasionally seen in individuals treated with steroids. Prior to the antibiotic era, pyemia was noted particularly as a complication of staphylococcal disease and resulted in multiple abscesses throughout the entire body, involving the heart or pericardium, and resulting in findings suggestive of myocardial infarction. In the brain pyemia caused multiple abscesses with and without meningeal involvement. In the lung one can see varying-sized pulmonary abscesses extending from very small abscesses to larger coalescent ones. The patient had a problem in the left base which might easily have been a series of abscesses from this process. The kidney is frequently involved, and this man did have pseudomonas in his urine in low numbers.

In this patient the organism responsible for pyemia could be *staphylococcus,*

and I think this *is the most common source of multiple abscesses.* He was never treated for his staphylococcal disease as adequately as we would like, and about the time of his operation he was getting nothing to counteract staphylococci. However, I am going to vote against staphylococcus because staphylococcal disease will usually not spread even though inadequately treated. It may enlarge and increase in the immediate area, but I would not expect new abscesses to develop. I am going to vote for pseudomonas just because it is a favorite organism of mine and because it appeared in the urine; I have seen pseudomonas act exactly this way on a number of occasions. It can spread. I have observed it in the heart and in the lungs, in the brain, and frequently in multiple liver abscesses. *Therefore I think pseudomonas is the most reasonable explanation for this man's disease.*

Steroid Therapy

This man needed steroids. We have to grant that steroids may have prevented long-term disability, and perhaps his eventual course was preferable to increased disability due to rheumatoid arthritis. However, when he came into the hospital with staphylococcal septicemia, I suspect that he might have done a little better if his steroid medication had been increased. A steroid dosage of 50 mg. a day is rather small. I would suggest that, since the life of solucortef is quite short, it might have been better to give him multiple doses rather than one shot a day. Then terminally, when he was getting very sick, I should think his dose would have been increased.

Antibiotic Therapy

The patient was known to have a staphlylococcal bursitis and a staphylococcal septicemia, but staphylococci were not cultured from the ankle. However, he had a clearly septic arthritis in the ankle with involvement of the bone, for which he received 500 mg. of prostaphlin q6hours intravenously. This is a dose that is used for minor infections. I myself would never use such a small dose because I don't treat trivial infections with antibiotics. I note that the penicillin dosage was much more reasonable; however, the organism was resistant to penicillin. In any event, he was sent home on prostaphlin alone. The total length of treatment was only three weeks. Osteomyelitis ordinarily should be treated for a number of months, if not years. In the treatment of his joint problems, the dosage was too little and the time too short.

Later the patient began to have abdominal problems and was given tetracycline and gantrisin. By this time, his condition must have become critical. I would strongly recommend using bactericidal drugs when a patient on steroids has a complicating infection. There was a period when this patient was getting only gantrisin and nothing for his staphylococcal disease or his diverticulitis.

Postoperatively he was treated with keflin 6 grams per day, which is certainly the least I would use for a patient this ill. Then Kantrex 450 mg. a day, which is the recommended dosage for a 30-kilogram man. This patient weighed more than that, the usual dose of Kantrex being 15 mg. per kilogram. Next he was placed on colymycin, 5 mg. per kilogram, a dosage appropriate for a desperately ill man. The dosage was then cut in half, which is not enough. I rushed to the laboratory values to see if he was developing elevation in his blood urea nitrogen as a result of the reduced dosage; however, that was not the case. He was finally placed on an adequate dose of keflin therapy prior to death; but by this time, if you will look on the sensitivity sheet, the organism was resistant to keflin. About the total antibiotic therapy; it appears that no one examined the whole spectrum of the disease and planned its progressive therapy.

Importance of a Lumbar Puncture

My next comment is directed to the fact that the patient became extremely disoriented about a week before he died. No lumbar puncture was done. The man was quite ill and had a number of reasons for developing mental symptoms such as anoxia and a low serum sodium. When a patient has evidence of generalized infection and develops mental symptoms, I would encourage a lumbar puncture. Certainly a complete neurological examination and a lumbar puncture are indicated in a case like this. Though our patient may not have had brain abscesses, such a possibility should nevertheless have been ruled out by a lumbar puncture. If he had pseudomonas in the meninges, of course, parenteral colymycin would not be effective and he would have had to be treated intrathecally.

My *final diagnoses* are (1) rheumatoid arthritis with staphylococcal pyarthroses involving the right wrist, left ankle, and pre-olecranon bursae and osteomyelitis of the spine; (2) diverticulitis with a pelvic abscess; (3) adrenal atrophy; (4) pyemia with metastatic infection of the heart, the lungs, the brain, and multiple other organs, probably due to pseudomonas species.

Pathology

Robert L. Strom, M.D.

It is a pleasure to have Russell back with us. We have been involved in a lot of verbal jousting about antibiotic therapy and I am sure this will resume and stimulate interest in the proper treatment of infectious disease in the institution. In defense of the antibiotic therapy, in the initial cultures on the joint there was also an anaerobic streptococcus and, because of this, the penicillin in high dosage may have been given mainly for this anaerobe. I think the anaerobic streptococcus again would suggest the possibility of an initial focus of infection in the colon, with extension into the blood stream and secondary infection of the joints.

Clinicians are very vigorous in their therapy with cortisone drugs which, in many cases, are a two-edged sword. Steroids are very helpful in relieving symptomatic discomfort; however, there are inherent risks and we must be ever alert for complications of steroid therapy.

This patient was extremely emaciated, weighing only 95 pounds. There were findings of the rheumatoid arthritis and evidence of a pelvic infection with drains in the pelvic region. The heart weighed 400 grams. Subendocardial hemorrhage was present, but no frank coronary thrombosis or myocardial infarction was found. We were interested in the myocardial process since the diagnosis of non-transmural myocardial infarction was made. The myocardial muscle itself looks quite normal but you will notice there is a perivasculitis. *Chronic myocarditis was present and this probably caused the electrocardiogram changes.* In addition, the patient had long standing rheumatic disease and we saw occasional small foci of perivascular scarring consisting of round cells with focal areas of fibrinoid change consistent with rheumatoid changes in the heart. There was no evidence of septic abscesses in the myocardium.

The lungs weighed approximately 1,000 grams combined weight and there was evidence of a *bronchopneumonia localized mostly to the left lower lobe.* The pneumonia apparently had been treated and was undergoing some resolution. I see no specific organisms or granulomas in the lung and I would assume that the infection in the lung represents a pyogenic rather than a mycotic infection.

The next thing that attracted our attention was heavy *pelvic adhesions in the area of diverticulitis.* Though this man had had a transverse colostomy, the infection did not totally subside. The cause of the bladder obstruction was a heavy infection of the prostate gland. Sometime prostatic gland infection leads to severe bladder neck obstruction. This infection of the prostate gland could be characterized as a

granulomatous prostatitis. One can see a number of granulomata in these areas of infected granulation tissue in the prostate itself. As we study the prostate in closer detail, much to our surprise we see lacunar spaces with small yeast-like organisms (Figure 2). There were 20,000 yeast organisms in the urine culture and I don't believe we followed up on them bacteriologically; I think we assumed they were Candida species. Closer observation of this infected prostate reveals a giant cell reaction and some mucopolysaccharide material within the giant cell reaction. A muci-carmine stain of the prostate shows multiple small budding yeast organisms which measure about 5-7 micra and are distributed throughout the prostate. These yeast organisms also take a PAS stain very vividly and, on this type of evaluation, one could consider a Candida or Cryptococcus type of organism. With the muci-carmine stain, however, the presence of a muci-carmine capsule suggests *cryptococcal prostatitis.*

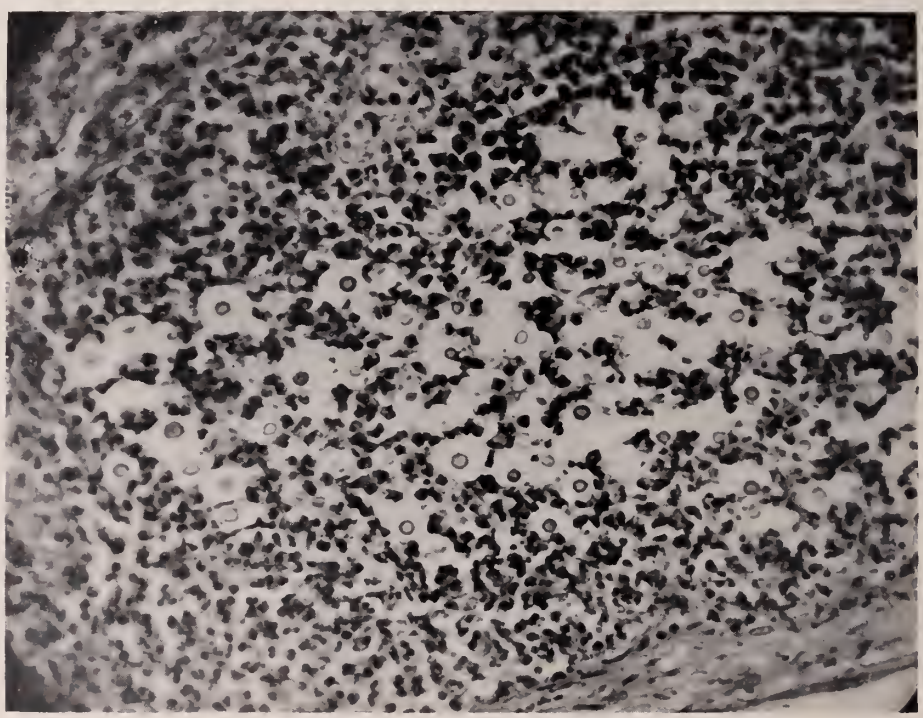


Fig. 3-X1000 Cryptococcal Meningitis.

Cryptococcal Meningitis

No spinal tap was done on this patient. He had symptoms of mental deterioration and confusion. If a spinal tap had been done, we would have seen on the India ink preparation the presence of budding yeast organisms with capsules around them diagnostic of cryptococcal meningitis. Individuals with cryptococcal meningitis have elevated spinal fluid cell counts, primarily of a lymphocytic type; an elevation of spinal fluid protein and a decrease in cerebrospinal fluid sugar. Spinal fluid cultures grow out Cryptococcus neoformans. This organism forms a mucoid colony much like Candida albicans. The fungi are easily differentiated by the production of urease by Cryptococcus neoformans.

Cryptococcus neoformans is responsible for a number of infections while patients are on steroid therapy. *When patients are infected with cryptococcal organisms, the mortality rate is extremely high.* Characteristically, the meninges are milky white, and fluid tends to loculate over the surface of the brain. When the brain is sectioned, one can see zones of necrosis extending in and around the cerebral sulci, into the basal ganglia, and surrounding the cerebellum.

In this case, a purulent meningitis was present, with many round cells and plasma cells, and within them we see yeast organisms (Figure 3). The meningitis surrounded the cerebral cortex and was most marked over the cerebellum. Within the purulent meningitis around the brain you can observe the red-staining PAS positive organisms in the meningitis. Such budding yeast organisms are characteristic of Cryptococcus neoformans.

Epidemiology of Cryptococcal Infections

Now for a few general comments about cryptococcosis. Approximately two thirds of these cases occur between the ages of 30 and 50 years. There is a very high incidence in white males and, in one series of 101 cases of cryptococcosis reported, 87% were in white individuals and 82% in men. *The reservoir for the infection is pigeon excreta.* We don't know the nature of our patient's occupation. Perhaps he was old enough to have spent a lot of time in the local parks and may have come in contact with pigeon excreta. Chester Emmons, who has done a number of epidemiologic studies of Cryptococcus organisms in soil, states that pigeon excreta contains up to 5 million Cryptococcus organisms per gram: a very potent source of infective organisms in the environment. Even in urban areas Cryptococcus can be prevalent because there are lots of pigeons and people have a tendency to protect them.

Cryptococcosis is an occupational disease in individuals who are pigeon tenders; but for some reason the Cryptococcus does not overtly infect the pigeons themselves. They carry it around their feet and on their bills but you do not find lesions of Cryptococcus in the pigeon flock itself. Obviously, it is in the gastrointestinal tract of pigeons and is being excreted. It has been said that possibly the high body temperature of the pigeon may account for the absence of organism growth.

Small white mice have been infected with Cryptococcus and this is a way of verifying the diagnosis. Cryptococcus is injected intracerebrally and, if you give the mice a little steroid, it helps the infection along very nicely.

We were slow to realize that individuals have a normal serum factor which is effective against Cryptococcus and that individuals on steroid therapy do not have this normal serum factor, as the therapy tends to deplete the factor. There are many predisposing factors of Cryptococcus infections; the most prominent ones we see clinically are Hodgkin's disease and lymphoreticular disorders. In a large series of cases up to 30% of the individuals with cryptococcal meningitis had Hodgkin's disease.[1] Leukemia, sarcoidosis, diabetes mellitus are frequent accompanying diseases. Rarely, rheumatoid arthritis and cirrhosis are associated with cryptococcosis, but in a case series studying the potentiation of cryptococcal infections with steroids, there were two cases of rheumatoid arthritis in six deaths reported. Generally these cases have had prolonged steroid therapy and the meningitis may be chronic; as the infection may last up to six months we have a good opportunity to positively diagnose it. Occasionally it is fulminant, as it apparently was in this case. This individual died perhaps two weeks after the onset of the headache and confusion.

These patients frequently have a primary focus in the lung due to Cryptococcus. The portal of entry is usually the lung with a hematogenous dissemination in the central nervous system. The prostatic infection in this case is of interest because of the intimate relationship between the venous plexuses of the prostate and the spinal canal and central nervous system. Because of this anatomic relationship the prostatic infection could have acted as a portal of entry to the central nervous sys-

tem. Our final pathologic diagnoses are (1) acute meningoencephalitis and acute prostatitis due to Cryptococcus neoformans; (2) bronchopneumonia left lower lobe; (3) chronic myocarditis due to rheumatoid arthritis; (4) chronic deforming rheumatoid arthritis; (5) acute pyogenic arthritis, left ankle, due to staphylococci.

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Book Reviews

A book may be as great a thing as a battle.—Benjamin Disraeli,

PHYSIOLOGY OF WORK CAPACITY AND FATIGUE—Edited by Ernst Simonson. C. T. Thomas. Springfield, Ill. 571 pp., 1971. Cost: $33.50.

Ernst Simonson, professor emeritus of physiological hygiene, University of Minnesota and professor emeritus of physiology, Frankfort/Main, Germany, has had a lifelong and world wide interest in fatigue. He and a distinguished group of collaborators have gathered here in this book a comprehensive text on the subject with a bibliography of over 1500 titles. Undoubtedly the standard text on physiology of fatigue for this decade will be this work. Although the general nature of fatigue is well recognized, there are many features that are obscure. Theories of fatigue are discussed especially accumulation of substances producing fatigue and depletion of substances essential for activity.

This work is planned as one unit of a trilogy; the other subjects for future consideration being the psychology of fatigue and performance and fatigue in disease. Dr. Simonson currently is director of medical electronic research at Mount Sinai Hospital, Minneapolis.

Reuben Berman, M.D.
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HAZARDS OF MEDICATION; Author: Eric W. Martin, Ph.D.; Publisher: J. B. Lippincott Company, East Washington Square, Philadelphia, Pa. 19105; Pages: 895; Price: $27.50.

This book does indeed epitomize an overwhelming mass of literature on the subject of medication hazards. It comprises 10 chapters, which cover essentially the entire field of hazards that might be anticipated.

It is a volume that should be available on the doctor's shelf for ready reference in all instances wherein a medical incompatibility has developed or might be anticipated.

The Table of Drug Interactions is in itself comprehensive, its value appreciable, however, only when it is needed.

The book does not deal with clinical manifestations or symptoms associated with incompatibilities, but principally with the characteristics of the drug itself.

The volume's greatest value is that of reference.

Carl O. Rice, M.D
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CLINICAL OTOLOGY: Paparella M, Hohmann A, Huff J: An International Symposium. St. Louis, The C. V. Mosby Company, 249 pp., 1971, Price: $29.50.

Paparella, Hohmann, and Huff bring together in print the spirit and content of the University of Minnesota's international symposium of clinical otology held in June 1971. The subject matter represents the text of papers and the dialogue of televised surgical procedures of that meeting. As the input for this book was designated primarily for a symposium, the material is rather loosely arranged and is held together only by reference to the broad arena of otology and otologic research. For example, Huff's chapter on the preoperative preparation for ear surgery is followed directly by practical clinical audiology, trends in audiology, research findings of another audiometric test called stereoaudiometry, and then back to surgery for restoration of hearing. The subject arrangement makes the book more a collection of monographs than a text of clinical otology.

The attitudes surrounding the controversial areas of otologic surgery are colorfully and vividly communicated by the late Fred Guilford's discussion of current trends in tympanoplasty and is seconded by Schuknecht's comments on tympanoplasty. Both men had devoted much of their careers to the establishment of the principles of surgery for chronic suppurative ear disease. Perhaps they give themselves too little credit for systematizing these attitudes, with a dual emphasis on eradication of disease and the reestablishment of the mechanism of sound conduction. Both of these are worthy goals, neither exclusively paramount, and Guilford and Schuknecht have been extremely active in maintaining a reasonable perspective during a period of rapid change in otologic surgery. Their historic overview, their awareness of the false starts and haphazard trial and error methods of investigation, is nowhere better stated than in this collection of comments and surgical vignettes on tympanoplasty. Nevertheless, their dismay at the trends and anxiety over the mechanisms of teaching otology seem a bit overstated.

The price of this book is justified by the extra-ordinary assembly and correlation of history, physiology, and anatomy and ideas in H. L. Williams' contribution, "The Anatomic Principles of Mastoid Surgery." He ties together the speculation, observation, and controversy that sound the fundamental question of "Why the Chronic Running Ear?" This is Williams in print at his very best.

A clue to the next frontier of otology—the problem of sensory neural deafness—is provided by the final one fourth of the collective papers. Schuknecht's work on diseases of the inner ear, Duvall's work on sudden deafness, and Cody's work on treatment of sensorineural deafness provide a neat trilogy on this subject.

The text is a souvenir for those who attended the symposium and should be read by aspiring and practicing otologic surgeons. Medical students and nonotologic physicians would be confused, however, if they approached "Clinical Otology: An International Symposium" as a text of clinical otology.

Lawrence W. DeSanto, M.D.*
Rochester, Minnesota



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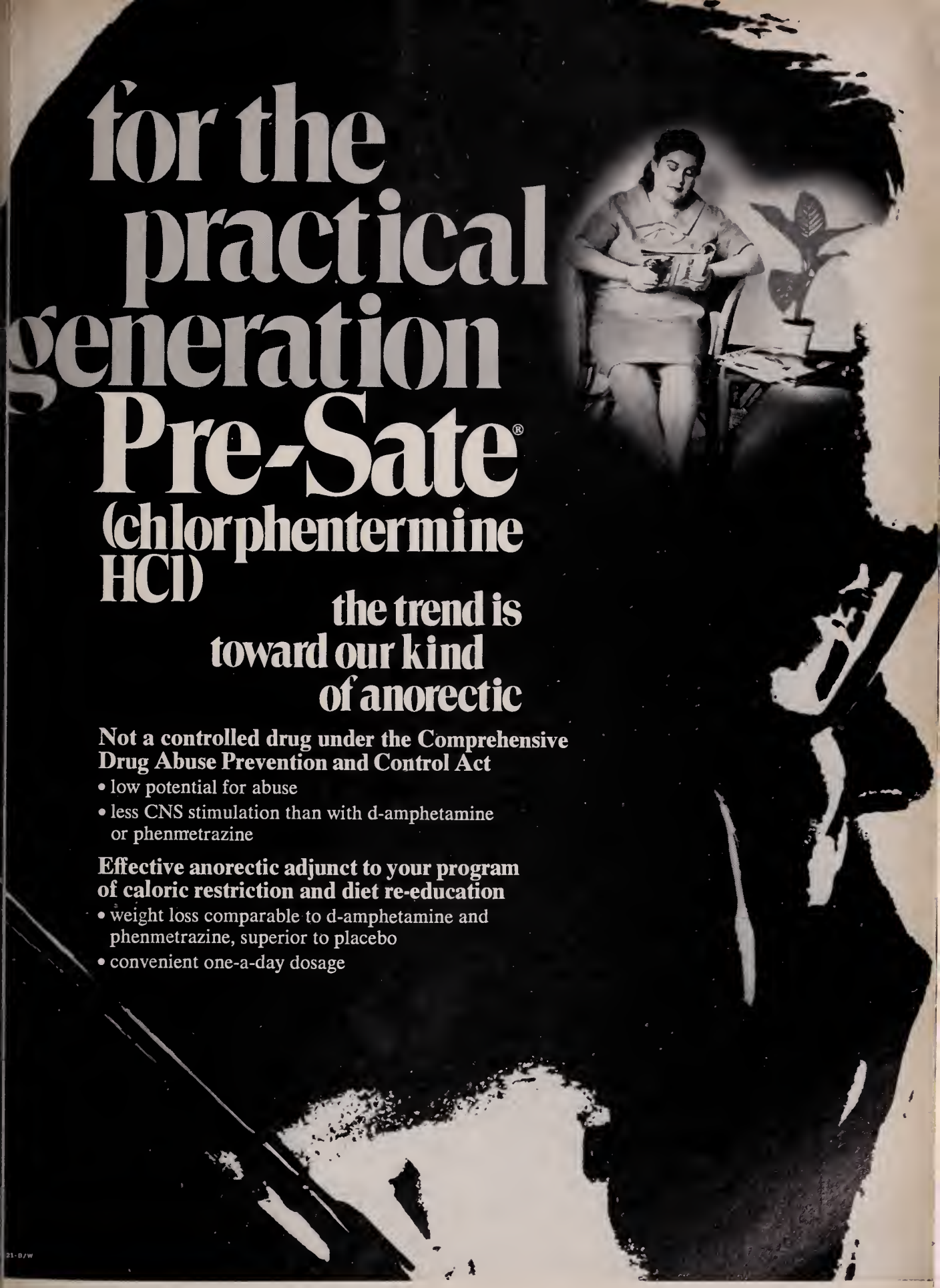
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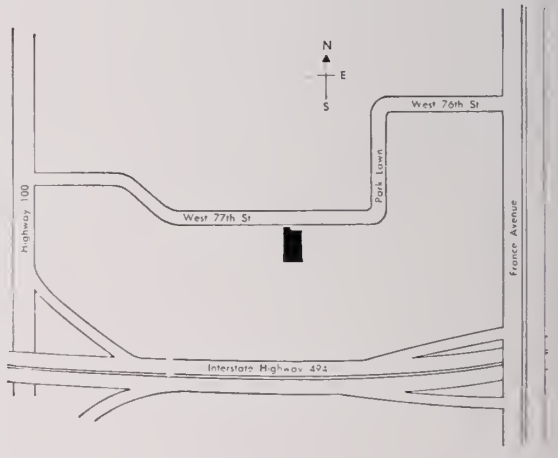
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President's Letter



People

THE COMPOSITION of one's first public message to his peers as President of our Association causes a great deal of contemplation on many critical and potentially explosive problems currently facing all of us. What should a president do? Be a strong outspoken leader gathering his followers for battle? Be cautious, play it cool, issue the old time-worn platitudes and cliches? None of these seem appropriate now.

For right at this time, I am feeling sympathy for those of our fellow humans who for one reason or another, i.e. lack of health education, transportation, poverty, etc., cannot find or properly utilize existing medical and health care. I feel angry at those who expolit this situation for personal or political gain and I feel compassion for all who are honestly trying to find solutions. The frustration resulting from fatigue and hopeless striving to care for more and more people and the agony of re-evaluating medical and health manpower education and its distribution are no strangers to me. I am aware of the feeling of responsibility also. The responsibility to do what is possible to fulfill the purposes stated in the Minnesota State Medical Association constitution, "the purposes of this corporation shall be community welfare, community health and scientific education—promoting the science and art of medicine, elevating the standard of medical education so that the profession shall become more capable and honorable within itself and more useful to the public in the prevention and cure of disease and adding to the comforts of life;—prevention of disease and promotion of the public health; assisting officials and agencies of the state of Minnesota with advice and service in the administration of its medical, hospital, welfare and public health programs; promoting high standards of medical and health service in all public programs established for the welfare of the people of Minnesota," so it appears that it is people and their quality of life that our Association is dedicated to by promoting the art and science of medicine.

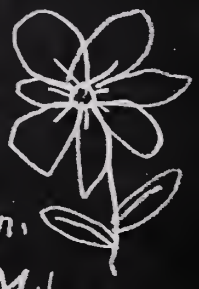
My message to you then is PEOPLE! Human beings with all their strengths and frailities; human beings, the beginning of each a point in time and the demise likewise, and their course and destination can only be surmised. Shall we share this humanness, you and I? Sharing our concerns may alter the course and increase the quality of time between the beginning and ending, the period we call life, for us and those we touch. I believe this to be true. I believe that this is what being a physician is all about.

George B. Fratten

President
Minnesota State Medical Association

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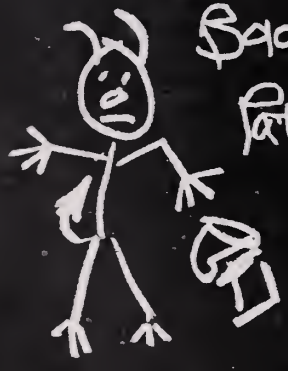


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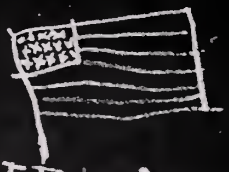
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Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

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Yes, it would be useful.

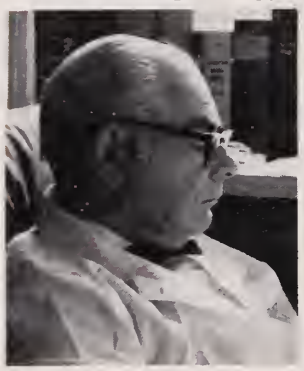
86.7%
No, it would not be useful.

Dialogue

Would it be useful in clinical practic to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy in practice can really determined.

The Bureau of Drugs suggested the package sert as a possible mean communicating informa on relative efficacy of d to the physician. I find objectionable, since I not believe the physi should have to rely on source for final scien truth. There is also a p tical objection: Since physicians actually pense drugs, they sel see the package insert any event, I would m tain that the physic should know what dru wants and why without pending on the governm or the manufacturer to him.

Undoubtedly, physic are swamped by exces numbers of drugs in s therapeutic categories. I am well aware that m drugs within such c gories could be elimin without any loss, or haps even some profit the practice of medic But, in my opinion, nei the FDA nor any o single group has the ex tise and the wisdom ne sary to determine the "drug of choice" in areas of medical practi

Maker of Medicine

Kenneth G. Kohlstaedt, M.D.,
Vice President,
Medical Research,
Eli Lilly and Company



In my opinion, it is not the function of any government or private regulatory agency to designate a "drug of choice." This determination should be made by the physician after he has received full information on the properties of a drug, and then it will be based on his experience with this drug and his knowledge of the individual patient who is seeking treatment.

If an evaluation of comparative efficacy were to be made, particularly by government, at the time a new drug is being approved for marketing, it would be a great disservice to medicine and thus to the patient — the consumer. For example, when a new therapeutic agent is introduced, on the basis of limited knowledge, it may be considered to be more potent, more effective, or safer than products already on the market. Conceivably, at that time the new drug could be labeled "the drug of choice." But as additional clinical experience is accumulated, new evidence may become available. Later, it may be apparent that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audiovisual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use — information that the pharmaceutical manufacturers must begin to provide if government regulation of *"drugs of choice"* is to be avoided.

Opinion & Dialogue

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Idiopathic Scoliosis

Current Concepts in the Treatment

ROBERT B. WINTER, M.D.,* and JOHN H. MOE, M.D.†

SCOLIOSIS, ONCE considered the scourge of orthopedics, has entered a new phase. In the past, treatment of this condition was so poor that one could only stand by and watch the curve get worse. Finally, when it got bad enough, a difficult fusion operation was done as a last resort. Such pessimism no longer has a place in the treatment of this condition, and the entire concepts of treatment have changed within the past ten years.

History

Before 1900 the only treatment for curvatures of the spine was various exercise programs. These did little to correct or prevent progression of these curvatures. The benefit derived from them was that both doctor and parents thought that something was being done. Subsequent studies, particularly those of the subcommittee of the American Orthopedic Association in the 1940's, proved conclusively that exercises *alone* do not affect either the severity or the progression of curvatures of the spine in the growing child.

Hibbs in 1911 published a paper on fusion of the spine for tuberculosis. Within a few years the same operation was adopted to the treatment of curvatures of the spine. Over the years there was a gradual acceptance of spine fusion as a satisfactory method of treatment for curvatures of the spine. Various refinements in casting and fusion technique evolved through the efforts of such men as Cobb, Risser, and Von Lackum. Thus a good method of treatment of a sufficiently developed curvature became available. The problem was that there was no treatment for the mild curve until it reached the point where surgery was considered indicated.

In the late 1940's Blount and Schmidt of Milwaukee began designing the Milwaukee Brace. At first, it was used only as a recumbent postoperative frame particularly for patients undergoing spine fusion for poliomyelitis scoliosis. In the 1950's it became apparent that when properly made and properly applied this brace was effective *as a non-operative, ambulatory method* in the treatment of idiopathic scoliosis.

About 1960 Paul Harrington of Houston, Texas, developed a set of instruments to facilitate the internal correction and internal support in the process of spine fusions. These are universally known as Harrington instruments, and have become widely used as a part of the fusion operation.

General Aspects of Idiopathic Scoliosis

Idiopathic Scoliosis, as its name implies, has escaped adequate knowledge as to the specific nature of the condition. However its clinical features are so well known and follow such characteristic patterns that its definition as a specific disease entity cannot be questioned. Prior to the use of vaccines, it was thought to represent a "subclinical" case of poliomyelitis. There has been no diminution in the incidence of idiopathic scoliosis through the use of poliomyelitis vaccines, and this theory must be discarded. Other authors have felt that dietary abnormalities and restrictions were etiologically significant. This seems to be ruled out by the consistency of the disease in countries of varying socioeconomic backgrounds and dietary conditions.

Classification

Idiopathic Scoliosis is divided into three categories based on the age of appearance.

1. *Infantile,* appearing under the age of three. This type is rarely seen in the United States, but is frequent in Great Britain and of Europe. It is usually a curve to the left, usually in boys. In 90% of cases it is self-curing in which case the curvature is gone by the age of two. Ten per cent of the curves progress, are not self-curing, and become severely crippling conditions, requiring

From the Scoliosis Service at Gillette Children's Hospital.
*Medical Director, Gillette Children's Hospital, and Associate Professor, University of Minnesota, Department of Orthopedic Surgery.
†Chief of Staff, Gillette Children's Hospital and Professor of Orthopedic Surgery, University of Minnesota.
See editorial, page 562.
Requests for reprints address to: Dr. R. B. Winter, Gillette Children's Hospital, St. Paul.



Fig. 1A—A female age 12.



Fig. 1B—The same girl two years later, no treatment having been given. Such progression should not be permitted.



Fig. 1C—Her mother.



Fig. 1D—An Xray showing her correction 15 months after surgery.

prolonged and aggressive treatment.

2. *Juvenile,* appearing between the age of three and puberty. This is a relatively less common time for the appearance of this disease; however, when it does occur, it is never self-curing, and because of the many years of growth remaining, tends to produce a very unsightly and crippling condition. Again, aggressive and unrelenting treatment is necessary.

3. *Adolescent,* appearing between puberty and the completion of spinal growth. In the United States, this is the most common type. Contrary to infantile idiopathic scoliosis, adolescent idiopathic scoliosis occurs almost exclusively in girls, and most commonly produces a right thoracic curve. It is usually steadily progressive from the time of appearance until cessation of spinal growth, usually about age 16 or 17. Since there are a fewer number of years in which this progression can occur, the final result is usually not as catastrophic as with juvenile or infantile idiopathic curvatures. Nevertheless, significant deformities occur, and treatment cannot be ignored.



Fig. 1E—The patient age 14, just prior to surgery (left) and (right) 15 months after surgery.

Complications

In addition to the cosmetic deformities produced by these curvatures, it has become increasingly apparent that significant alterations in the pulmonary function and cardiac status can result from curvatures of the spine. Deformity of the thorax results in a loss of usable lung space, and secondarily results in a shunting of blood through the pulmonary circulation without adequate oxygenation. Pulmonary function studies in the past have been too unsophisticated to detect these early abnormalities, but recent techniques measuring intra-arterial oxygen tension and perfusion-ventilation studies using radioactive xenon, have shown these defects in pulmonary physiology much earlier and with much smaller curves. A recent study by Nachemson in Sweden has shown that there is a 100% increase in mortality in patients with thoracic scoliosis after the age of 40.

Genetics

Dr. Ruth Wynn-Davies of Edinburgh, Scotland, showed in a general population study of 11,000 Edinburgh School students, that there was an incidence of early onset scoliosis (under the age of eight) of 1.3 per thousand students. Late onset scoliosis (over the age of eight) occurred at an incidence of 1.8 per thousand students. Of those patients with scoliosis, all of the first, second, and third degree relatives were examined, a study of over 2,000 individuals. Approximately 25% of the patients had a positive family history of scoliosis. The genetic factor appeared to be stronger for the late onset scoliosis than for the early onset scoliosis.

Drs. Cowell, Hall, and MacEwan from DuPont Institute, Wilmington, Delaware, showed in a recent detailed study of 100 families in which one child had scoliosis, that in eighty per cent of the families a sibling or parent had scoliosis. Many of these were not aware that they had a curvature, but when Xrayed, were found to have this condition. There appeared to be a sexlinked dominant mode of inheritance, as there was no male to male transmission documented. It seems evident, from these studies, that a strong genetic factor is present in this disease.



Fig. 2A—A 13-year-old female with a 100° curve from the fifth thoracic to the first lumbar vertebra.



Fig. 2B—The same girl at age 17, four years after surgical correction of the deformity.

Treatment

There are three ways to treat these curvatures. The *first* is to do nothing, except to observe the child periodically, including the taking of Xrays to see whether a curve is present, or if present, whether it is progressive. This type of "observational treatment" is rarely justifiable. *As noted previously, physical therapy and exercises do not, have not, and never will correct an already present curvature of the spine.* Exercises *are* important when properly combined with a Milwaukee Brace or fusion program.

The *second* form of treatment is fusion. This has definite indications, and is used when the patient presents already having completed growth, and with sufficient deformity so that treatment is necessary. The Milwaukee Brace is not effective in treating the fully grown individual. Fusion remains the only available choice for this type of patient. The second indication is the patient with a curvature that is beyond the ability of the brace to treat. These sometimes require fusion, regardless of the age of the patient.

Arthrodesis of several segments of the spine (the fusion operation) plays an important part in the treatment program. Unfortunately, many children do not have their curvatures detected by their parents or family physician until they reach



Fig. 2C—Her appearance (left) just prior to surgery and (right) four years after surgery. She spent nine months in a cast.



Fig. 3A—A 15-year-old male with a double curve pattern, right thoracic and left lumbar.



Fig. 3B—The same boy three years later at age 18. Surgical correction by Harrington Instrumentation and spine fusion T3-L4.

a serious degree of curvature. At other times, even more unfortunately, the pediatrician or family physician will note the presence of a curvature and state "it isn't so bad, and I don't think it will get worse", only to have the child come to the orthopedist several years later with a crippling deformity. Advances in the fusion operation are primarily those of the Harrington instruments for gaining internal correction and internal stability. This has provided a lowered incidence of pseudoarthrosis and permit early ambulation. We are now ambulating most of our patients in casts as early as six days after surgery, compared to our previous practice of keeping patients in bed for six months. Even with the instruments it is necessary to keep the patient in a cast for at least nine months after the operation.

The *third* form of treatment is the use of the Milwaukee Brace. This brace has proven very effective in the treatment of idiopathic curvatures, *providing that the cihld is still growing,* and *that the curve is not too severe.* The Milwaukee Brace has become an increasingly important tool in the treatment of these curvatures. This has evolved from our greater understanding of its capabilities and limitations. It also evolves from our greater ability to make a good brace, and with greater

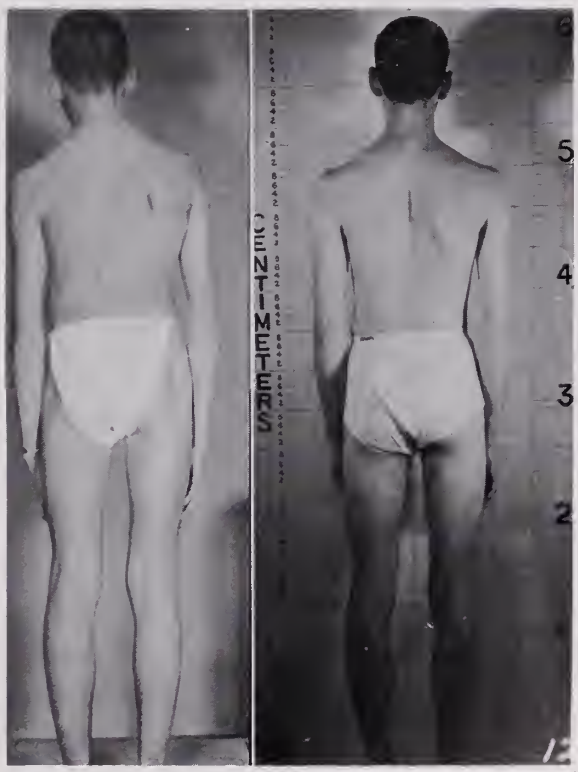


Fig. 3C—Preoperative photograph, age 15 (left) and postoperative photograph, age 18 (right).



Fig. 4A—A 10-year-old female with a progressive curve. The curve had measured 45° three months previously.

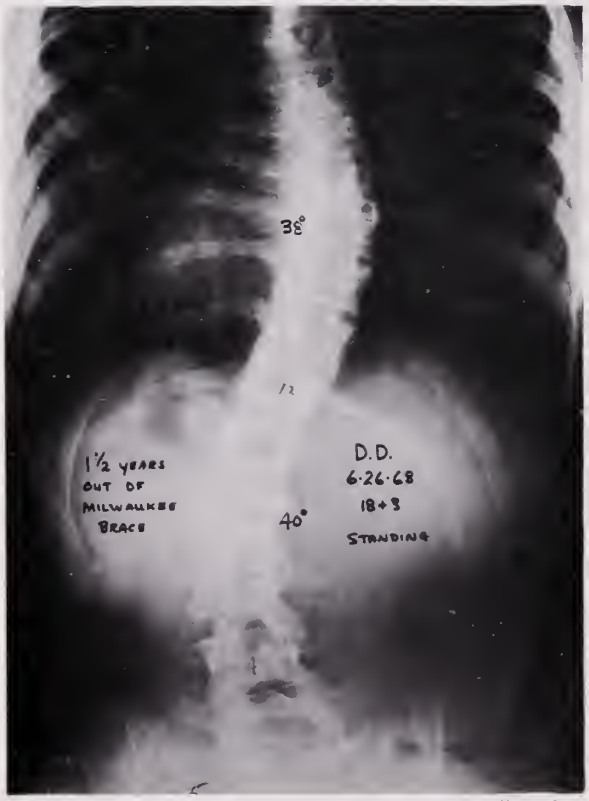


Fig. 4B—The same girl, age 18. She wore a Milwaukee Brace from age 10 until age 16.

understanding on how to use the brace. The brace will prevent progression of most idiopathic scolioses. Therefore, when applied *early enough,* worn *long enough,* and removed *slowly enough,* the curvature will be completely halted in its progression and never reach a significant degree of curvature.

The physician must apply the brace at a time when the curvature is minimal enough to respond to the brace. From a practical point of view, it has been our experience that almost no curvatures under 40° (by the Cobb technique) will ever require surgery, if properly treated with a Milwaukee brace. This is *not* to suggest that we wait until the curve reaches 40°. The brace should be applied when the curves are small, preferably when about 15°-20°. Under 15°, treatment is not justifiable and permitting a child to progress from 20°-40° before starting treatment is indefensible, since this progression can rarely be retrieved.

Discussion

Advances in the past ten years have removed most of the fears of idiopathic scoliosis. It has now become a treatable condition with a good prognosis. When detected early by routine examination of the spine by the family physician or the pediatrician, treatment can be instituted with a Milwaukee Brace. Providing that the patient is cooperative about wearing the brace, a good prognosis can be anticipated and surgery avoided.



Fig. 4C—Photograph of this girl at the time treatment was started (left). It is easy to see how these curves can be missed by casual observation. Her appearance at age 18 (right). She has no pain, no scar, normal spine motion, and was never hospitalized.

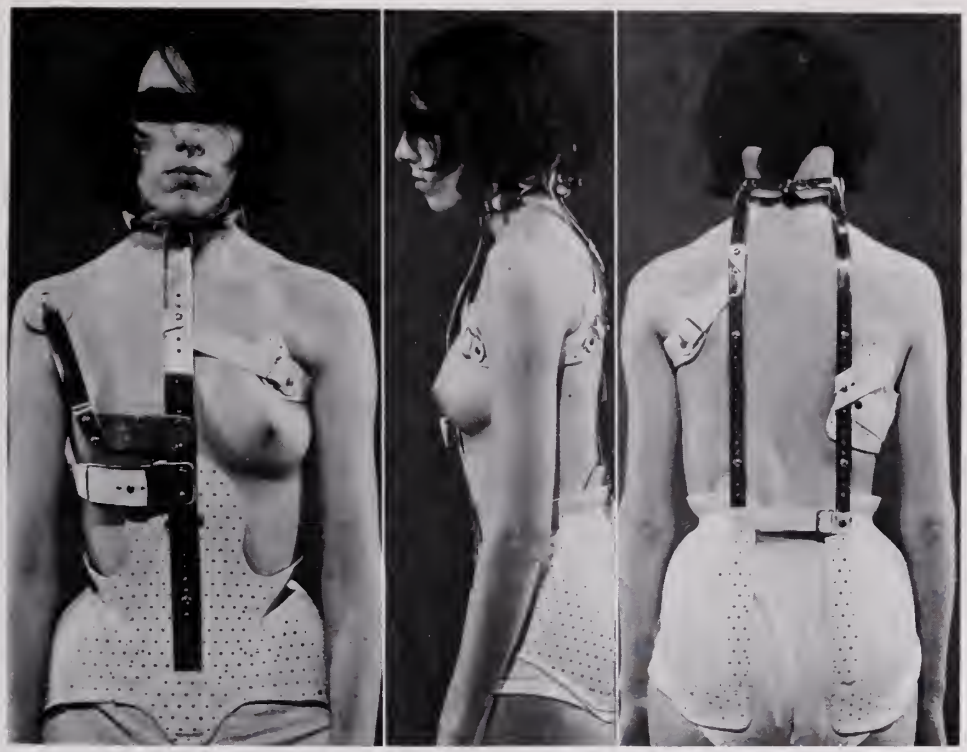


Fig. 5—A modern Milwaukee Brace. It is perfectly comfortable and causes no pressure on the teeth or jaw (a frequent criticism of earlier such braces). The child can participate in all activities except tumbling, trampoline, and football.

When the patient presents with an already significant deformity, beyond the ability of the brace to correct, good fusion operations are now available, and, again, a good prognosis can usually be rendered. A fusion is a serious, major orthopedic operation, and carries with it a significant number of complications. We feel the brace treatment is always preferable, providing the curve is responsive to the brace. In some instances, it is borderline whether a curvature will or will not respond to the brace. Under these circumstances, it is best to try the brace for six to 12-months, and if it fails, then proceed with surgery.

Summary

A better understanding of idiopathic scoliosis is now available, and the genetic nature of the disease has become increasingly obvious.

A pessimistic "watch and wait" attitude can no longer be condoned.

Early treatment of minimal to mild curves with the Milwaukee Brace has proven to be our most effective treatment. This gives the child a functionally excellent spine, an excellent cosmetic appearance, and avoids the need for extensive surgery.

When surgery is necessary, good technique has now given us a high rate of success, with a minimum number of complications.

The treatment of scoliosis has reached a new era, in which optimism and enthusiasm have now replaced the gloom and despair of former years.

Falstaff: Sirrah, you giant, what says the doctor to my water?

Page: He said, sir, the water itself was a good healthy water; but, for the party that owed it, he might have more diseases than he knew for.*

*Shakespeare: 2 Henry IV, I.ii.

Treatment of Bone Tumors in Children

MARK B. COVENTRY, M.D.*

Bone tumors in children present a problem not really different from that in adults. Certain tumors are more prone to occur in childhood and adolescence, and others more likely in later decades of life. The basic treatment, however, remains essentially the same regardless of the age of the patient.

Bone tumors are best considered in three groups: (1) benign tumors, (2) lesions that simulate benign tumors but that are not truly neoplasms, including unicameral bone cyst, aneurysmal bone cyst, fibrous dysplasia, and eosinophilic granuloma, and (3) malignant tumors, classified as accurately as possible according to cell of origin. There are some gray areas in this classification. Is osteoid osteoma truly a neoplasm, for example? The same question might be asked about fibrous cortical defect.

Benign Tumors of Bone

Osteochondroma (Osteocartilaginous Exostosis)

Commonly found at the juxtaepiphyseal area, osteocartilaginous exostosis is frequently multiple and is often familial. It is removed only if it is large enough to produce symptoms because of mechanical and factitial reasons, or if it is becoming disproportionately large. One cannot support the argument that all osteocartilaginous exostoses should be removed because they may occasionally become malignant. These tumors can be followed closely and, if growth occurs, removed. Removal should be adequate, with the base of the exostosis thoroughly excised. Occasionally this will entail use of a bone graft, for some of the bases are quite broad and the bone is weakened when the exostosis is removed.

Chondroma

This tumor is seen most commonly in the hands and feet, and does not become malignant. The chief problem is that of diagnosis. One can be relatively sure of the diagnosis from X-ray evidence alone, as the tumor has a typically clear, lytic, demarcated appearance. Contrary to the behavior of chondromas elsewhere in the body, those in the hands and feet do not seem to manifest an increased incidence of malignancy because of biopsy. If in doubt, a chondroma of the hand or foot can be subjected to biopsy and the site thoroughly excised by curet and bone grafted.

Chondromas elsewhere, in the long bones particularly, are not uncommon and typically contain flecks of calcium. These should not be subjected to biopsy unless they can be treated definitively, and definitive treatment means removing every portion of the tumor. Roentgenographic recognition is not difficult and such a tumor is best left strictly alone unless one can remove it entirely and be prepared to deal with the consequences as far as function of the limb is concerned.

Multiple enchondromatosis (Ollier's disease) presents a similar problem, and individual lesions that do become troublesome must be dealt with accordingly.

Benign Chondroblastoma (Codman's Tumor)

This occurs most commonly at the epiphysis of the long bones and is best treated by excision with curet and bone grafting. Recurrent growth or subsequent malignancy is not a problem.

Chondromyxoid Fibroma

This fairly rare tumor is best treated by excision and bone grafting.

Osteoid Osteoma

Seen commonly in children and adolescents, osteoid osteoma is one of the newer and exciting entities that has captured attention in the last 20 years. Often the diagnosis is obscure and one must exert considerable acumen to demonstrate the lesion roentgenographically after it has been suspected because of the history of pain, specifically relieved by aspirin. The treatment is surgical excision of the nidus. The tumor must be completely removed to assure a cure. Occasionally the defect is large enough to require bone grafting.

Benign Osteoblastoma (Giant Osteoid Osteoma)

This presents a problem in treatment because

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of its size. It may affect the flat bones of the pelvis or sacrum or the vertebral bodies. Complete excision is sometimes difficult. Some of these tumors, diagnosed by biopsy and not treated, have remained quiescent and stopped growing. Others have continued to grow. They are quite vascular and often difficult to remove. Excision by curettage, when possible, is recommended. Occasionally x-ray therapy also must be given to control growth.

Benign Giant Cell Tumor (Osteoclastoma)

This tumor is rare in the child and adolescent. It is one of the most difficult to treat because of its propensity to recur. All the cells must be removed by one means or another to effect a cure. Because it often affects the lower end of the femur and the upper end of the tibia, which are important weight-bearing structures, radical surgical treatment presents a problem regarding function. Segmental resection, when feasible, is the treatment of choice. When it is not, wide exposure with thorough excisional currettement and irrigation, followed by bone grafting, will often effect a cure. Occasionally one is fortunate enough to find the tumor at a site, such as the upper end of the fibula, that can be resected without sacrifice of function, or in the lower end of the radius, where the entire lower portion of the radius can be removed with the tumor and replaced with a bone graft. Timid inadequate removal of giant cell tumor simply is not effective and results only in recurrence and often, ultimate amputation.

Radiation therapy is to be condemned because of the subsequent change of malignancy.

Fibroma (Fibrous Cortical Defect)

In contrast to giant cell tumor, fibrous cortical defect needs no surgical treatment unless a pathologic fracture occurs. If the bone has been weakened by the cortical fibroma, bone grafting may be necessary, but usually healing occurs with the usual methods of immobilization and use of plaster casts, and no other treatment whatever is required. The important point is to recognize that the fibroma is benign, tends not to grow after full maturity, and will indeed ossify as time goes on. It occurs most commonly about the ankle, proximal to the epiphysis of the distal part of the tibia.

Hemangioma

This tumor may involve large parts of the shaft of large bones or the pelvis, or it may be confined to the vertebral centrum. No really satisfactory treatment is available. Wide excision and bone grafting may occasionally be required. Differences in limb length may occur because of the stimulation of growth by the hemangioma. Even amputation may be necessary at times. A hemangioma in a vertebral body usually needs no treatment and causes no particular disability.

Bone Lesions Simulating Benign Tumors

Solitary Bone Cyst

This is the most common lesion of bone that appears primarily in children. It occurs most often at the upper end of the humerus, but is found at many other sites. It is on the diaphyseal side of the epiphysis and defies easy obliteration, resembling giant cell tumor in its behavior. Surgical excision of the entire cyst and replacement with bone grafts is necessary. Then the patient must be followed carefully for evidence of recurrence. If the cyst does recur, it again must be excised and bone grafting done. There is no place for the use of x-ray therapy in treatment.

Aneurysmal Bone Cyst

A more recently described tumor, this is best treated by curettage and bone grafting of the defect. Such treatment will usually cure the condition, although recurrences are occasionally seen and should be watched for.

Fibrous Dysplasia

Part of a generalized process, fibrous dysplasia is not truly a bone tumor, but acts in this way and is sometimes large enough to weaken the long bone involved by it. It may require excision and bone grafting.

Eosinophilic Granuloma (Histiocytosis X)

This most often affects children—the ribs, skull, and vertebral bodies. When found in a vertebral body, it produces a classic coin-like collapse of the vertebral centrum—"vertebra plana," or Calvé's disease.[1] While formerly managed with x-ray therapy, in recent years there has been some observation that the lesions heal spontaneously. If not symptomatic, therefore, immobilization alone might be tried before irradiation is resorted to.

Malignant Tumors of Bone

Malignant tumors of bone are also best classified by cell of origin, and may be subclassified on the basis of radiosensitivity as follows: radioresistant tumors: osteogenic sarcoma, chondrosarcoma, fibrosarcoma, and malignant giant cell tumor;

radiosensitive tumors: myeloma, malignant lymphoma, and Ewing's tumor; and miscellaneous tumors: chordoma, adamantinoma, angiosarcoma, and liposarcoma.

All malignant tumors of bone affect children except possibly adamantinoma and myeloma. Osteogenic sarcoma, the most common, is of course the classic one of childhood. Primary malignant tumors of bone most often affect young, otherwise healthy individuals in the golden age of youth and development. Amputation, when anatomically possible, is usually preferred for radioresistant malignant tumor of bone, including osteogenic sarcoma, chondrosarcoma, fibrosarcoma, malignant giant cell tumor, and perhaps Ewing's tumor. Statistical evidence indicates that this is the best treatment for these tumors under usual circumstances.[2,3,4]

At what level should amputation be done? Studies at the Mayo Clinic have shown that the tumor extends, on the average, three inches up the medullary cavity beyond the level of cortical involvement that is obvious roentgenographically. So, to get above the tumor, one must leave a fairly wide safety zone, bearing in mind this factor of medullary extension. But there is no added safety in leaving a joint between the tumor and the site of amputation. The amputated specimen is carefully checked by the pathologist to make sure that the entire tumor has been removed grossly and that there is no medullary extension to the amputation site. The point is to remove the tumor completely.

Resection can be considered for certain selective tumors of the extremity. The decision whether to do a wide local resection depends on the degree of malignancy and the anatomic location. Parosteal sarcoma can occasionally be treated by local resection, but recurrence, if such happens, dictates amputation. Chondrosarcoma of low grade and involving a bone that can be resected without severe disturbance in function, such as the upper third of the fibula, can be so treated. Chordoma involving the sacrum is of low-grade malignancy and can be completely removed locally in some instances. Also, in special location such as the thoracic cage, resection is the treatment for radiosensitive tumors, not of choice, but of necessity.

Radiation may be used primarly for radiosensitive tumors or as an adjunct to definitive surgical treatment. Myeloma, especially the solitary type, may be considered a primary malignant tumor of bone for this discussion, though it is not in the same category as the others. It does respond to irradiation, as does malignant lymphoma (reticulum cell sarcoma). Ewing's tumor is relatively radiosensitive and our figures at the Mayo Clinic show approximately the same rate of cure with irradiation as with surgical treatment.[5] Specifically, in the treatment of Ewing's tumor, I believe that if the tumor has not progressed to the point of pathologic fracture or marked soft-tissue involvement, it may be treated by irradiation after the diagnosis has been confirmed by biopsy, and later, if no metastases appear and the tumor regresses, amputation may follow. This is particularly true of tumors of the upper extremity.

Combining irradiation with amputation seems to offer little to the patient unless the amputation has resulted in certain spillage of tumor cells. There then may be some rationale for following amputation with x-ray therapy.

We have not been convinced of the value of preamputation x-ray therapy. Francis[6] recently reported on 33 patients given preliminary x-ray therapy over a period of six to eight days. Amputation promptly followed completion of the irradiation. Seven patients are alive and well five years or more after treatment, giving a survival rate of 21.2%. This rate is similar to ours following surgical treatment alone. Preoperative irradiation delays definitive treatment, and the biopsy itself, performed before treatment is commenced, may be detrimental by enhancing metastasis. Those who advocate this form of therapy would have the patient wait six months or so after irradiation to see whether metastasis occurs and then give definitive surgical therapy if there is x-ray evidence of continued growth of the tumor or if pathologic fracture has occurred. There is as yet no evidence that preamputation x-ray therapy localizes or encapsulates the tumor and prevents metastasis.

The following plan of treatment, and the statistics, from Middlesex Hospital, London, where this method is being employed, is available.[7] Biopsy of the tumor is performed and supervoltage irradiation of the entire limb is begun the same day. The patient is treated five or six days a week for six to eight weeks. Roentgenograms of the chest are made frequently. If there is no

x-ray evidence of metastasis in six months and if there is Xray or other evidence that the tumor is still present, amputation is performed. Amputation may be delayed indefinitely.

Of 109 patients treated at Middlesex Hospital from 1950 to 1962, 26 had sarcoma in Paget's disease, 37 osteogenic sarcoma, 21 fibrosarcoma, and 25 chondrosarcoma. Fifty percent of these patients died of pulmonary metastasis, and in 90% the metastasis was evident one year or less after diagnosis. Surviving among those eligible for five-year follow-up were one of 19 patients with sarcoma in Paget's disease, seven of 30 with osteogenic sarcoma, four of 15 with fibrosarcoma, and seven of 17 with chondrosarcoma. Thus, the five-year survival rate in osteogenic sarcoma was 23%, which is comparable to the rates given in most reports on patients treated by amputation.

Oncolytic chemotherapeutic agents are being developed and used today. As yet there is no proof of their value. A program being conducted at the Mayo Clinic combines the use of actinomycin D with surgical treatment of malignant bone tumors. Statistically the findings are not as yet significant. Our preliminary impression is that this plan has not improved the survival rate. Perfusion is advocated and used palliatively in some centers for malignant bone tumors of the extremity when metastasis has occurred. Again there is as yet no evidence that it is helpful.

Statistics on survival indicate the effectiveness of treatment of primary malignant tumors of bone. Such statistics, to be meaningful, must be based on careful review of a large number of patients.

The survival rates for patients with malignant bone tumors encountered at the Mayo Clinic in the years 1909 through 1958 are given in the Table.

TABLE
Survival Rates for Patients With Malignant Tumors of Bone, Mayo Clinic, 1909 Through 1958

	% surviving	
Type of tumor	5 yr	10 yr
Osteogenic sarcoma	20.3	17.4
Chondrosarcoma		
Operation without entering tumor	76.4	69.2
Tumor cells "spilled"	38.0	18.6
Fibrosarcoma	26.8	...
Malignant giant cell tumor	29.0	...
Malignant lymphoma	34.8	...
Ewing's sarcoma	15.0	10.7
Solitary myeloma	53.0	44.0

Our views regarding treatment may be summarized as follows: Each patient presents a specific problem. Certain generalities can be applied to this patient in view of accumulated experience of ourselves and others. Amputation remains the treatment of choice in patients with primary malignant tumors of bone, which are generally radioresistant. Some respond to irradiation. While irradiation is not generally effective for certain tumors such as osteogenic sarcoma, chondrosarcoma, and fibrosarcoma, it occasionally effects a cure. The amount of irradiation necessary to destroy tumor cells, however, is certainly considerable, and usually results in destruction of the other soft tissues as well. We must give each patient the maximum benefit of surgical treatment as it applies in his individual case and to his particular tumor. We should guard against pessimism and should let large series of cases with adequate follow-up be our guide toward treatment. Although it is difficult to do an amputation because of the obviously deforming results, less radical measures are usually inadequate for radioresistant malignant tumors. A living patient without one of his extremities can be a happy person and a useful member of society.

It has often been said that osteogenic sarcoma is more virulent and more lethal in younger age groups. Hayles, Dahlin, and I[8] attempted to compare the survival rates in osteogenic sarcoma in children less than 16 years of age with the rates in older age groups. We studied the data on children seen in the 50-year period 1909 through 1958;[8] accurate follow-up information was available on 126 of 129. The five-year survival rate for patients less than 16 years of age was 22.2%. In the entire age group, 20.3% survived five years.[4]

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Fatal Neoplastic Pulmonary Embolism

During General Anesthesia

WEN Y. YUE, M.D.*

PULMONARY EMBOLISM constitutes one of the most dramatic and tragic events encountered in medical and surgical practice. Although the literature contains numerous descriptions of embolism caused by blood clots, air, fat, and amniotic fluid, tumor embolism occurs rarely. The following report describes a fatal case of pulmonary neoplastic embolism in a young man during general anesthesia and surgery for removal of an abdominal tumor.

Case Report

A 17-year-old male entered the hospital complaining of painful scrotal swelling of one month's duration. His referring physician had prescribed antibiotics without improvement. Examination showed an otherwise healthy young man with a firm tender mass measuring 5 x 6 x 5 cm. in the left scrotum, and a second mass "the size of an orange" in the left upper quadrant of the abdomen.

A left orchidectomy was done without complications; pathological examination of the specimen showed teratocarcinoma with embryonal carcinoma of the testicle. The postoperative course was uneventful. One week later, a lymphangiogram revealed blockage of the left lymphatic drainage, suggesting metastasis. A chest film showed a questionable small nodule in the right lower lung field. A liver and kidney scan appeared normal

A left radical thoraco-abdominal lymphangectomy was attempted one week later with removal of the tenth rib, exposing the left side of the abdomen as well as that half of the diaphragm. Tumor tissue found behind the transverse colon below the spleen and kidney contained the same type of neoplasma as found previously in the testis. Vital signs had been stable; surgical blood loss had been replaced with Ringer's lactate solution and whole blood up to this stage in the procedure.

Quite suddenly, during manipulation and separation of the tumor, the patient's blood pressure dropped precipitously, with slowing of the heart rate as shown by the electrocardiographic monitor. All anesthetics were immediately discontinued, while ventilation with 100 percent oxygen was maintained. Cardiac arrest occurred two or three minutes later. Direct cardiac massage was begun at once and continued for one hour and 50 minutes, accompanied by doses of sodium bicarbonate, isoproterenol, and direct current defibrillation. Following resuscitation, the patient bled profusely and expired 52 hours later.

At autopsy, the pathologist found tumor emboli in the left pulmonary artery and smaller branches of both lungs, fat emboli in both lungs, and a huge left hemi-abdominal hematoma.

Discussion

An embolism may be venous or arterial (pulmonary or systemic) in origin, but a combination of both conditions is possible in patients with atrial or ventricular septal defects. The overall incidence of all types of pulmonary embolus, as revealed in postmortem studies in this country, is about 10 percent.[1] Five cases of massive systemic tumor embolization during or following pneumonectomy have been reported in the literature.[2-5] Taber[4] suggested routine primary pulmonary vein ligation to prevent both macroscopic and microscopic tumor embolization at the time of pulmonary resection for malignancy.

Sudden or unexpected death due to pulmonary neoplastic emboli during or following operation has been reported previously in a total of only six patients.[6-11] Death in four of these occurred during operation; two patients developed pulmonary emboli following surgery. Five of the six patients had renal carcinoma; the sixth had carcinoma of the adrenal cortex. Our patient had teratocarcinoma with embrynal carcinoma of the left testis. Gordon-Taylor and others[12-17] have reported both systemic and pulmonary tumor emboli which appeared during the natural course of disease in unoperated individuals with testicular tumor and sarcomatous malignancy.

Early recognition of pulmonary embolism during anesthesia may be of the utmost importance. The two most prominent clinical signs are a sudden, unexpected drop in blood pressure and irregular breathing during manipulation of the tumor; these symptoms do not correlate with blood

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volume loss or replacement, or change with discontinuation of anesthesia. Respiratory arrest usually occurs promptly, followed by cardiac arrest. Sluggish response to vigorous cardiac resuscitation is also suggestive of pulmonary embolism. Bethune and Brechner[18] indicated that an abrupt fall in alveolar carbon dioxide may be the only sign of early or small-volume venous air embolism preceding the onset of systemic hypotension; they suggest the use of alveolar carbon dioxide monitoring for detection of massive air embolism during surgery. The same measure should aid recognition of any pulmonary embolus.

The coexistence of tumor and fat embolism in this case is another interesting finding. The source of fat could not be identified.

There is no specific effective treatment for pulmonary tumor emboli. If the embolism is massive, nothing short of embolectomy, with or without the use of extracorporeal circulation, would be of value. No one has reported such an application for tumor embolism, however. Supportive measures include the use of hypothermia, administration of steroids, maintenance of blood volume and adequate urinary output, and assisted or controlled ventilation.

Summary

This is a report of a rare case of fatal pulmonary neoplastic embolism occurring in a 17-year-old youth under general anesthesia during removal of a metastatic testicular tumor from the left upper abdomen.

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Diseases . . . crucify the soul of man, attenuate our bodies, dry them, wither them, shrivel them up like old apples, make them so many anatomies.*

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Gastrointestinal Malformations in Down's Syndrome

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IT IS THE PURPOSE of this paper to report the five year experience (1963-1968) at the University of Minnesota Hospitals with Down's Syndrome (D.S.) and gastrointestinal malformations.

Case Report

The patient was admitted to University Hospitals at the age of fourteen weeks with a two-week history of vomiting. A diagnosis of D.S. had previously been confirmed by chromosome studies (21 trisomy). Physical examination revealed a "peristaltic wave and olive" that characterizes pyloric stenosis. Fluid and electrolyte balance was achieved in the next twenty-four hours and a Ramstedt pyloroplasty was performed. His postoperative course was uneventful.

Presented, in part, at the Northwestern Pediatric Society, Hudson, Wisconsin on September 26, 1969.

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The above case revealed little in the literature concerning a possible association between D.S. and pyloric stenosis. No complete review addressing itself to the gastrointestinal abnormalities in Down's Syndrome has been reported.

Review of the Literature

The incidence of D.S. in the general population is 1/600 live births.[1] Table 1 shows the incidence per live births in the general population for the individual gastrointestinal malformations. Data support the premise that duodenal atresia,[12] annular pancreas,[11] and Hirschsprung's disease[16] have an increased incidence in patients with Down's Syndrome. Isolated mention of reports of tracheoesophageal (T.E.) fistulae,[23] pyloric stenosis[1,2] and imperforate anus[1,23] have appeared.

From Carter's study[1] which reviewed 725 D.S. patients and Hanhart's study[19] of 800 D.S. patients, the incidence of gastrointestinal malformations is estimated at 10 to 18%. Carter's figure of 10% is probably more accurate since it is derived from

TABLE 1

Summary of Down's Syndrome and Gastrointestinal Malformations at the University of Minnesota Hospitals 1963-1968:

Incidence: Down's Syndrome occurs 1:600 births. 10-18% have G.I. malformations 1,19. 12% in present series.

G.I. Malformation	Incidence per live births in general population	Incidence of D.S. with Specific Malformation: Literature	Present Series	Incidence of Malformation in Down's Syndrome— Present Series
Imperforate Anus	1/1500-5000[24]	8/198[23]	3/11	3/110
T.E. Fistula	1/1300-4500[24]	2/233[23]	1/16	1/110
Hirschsprung's	1/5000[17]	24/1163[17]	2/13	2/110
Duodenal Atresia/Stenosis	1/10000-40000[24]	150/503[12]	2/6	2/110
Annular Pancreas	1/10000-40000[24]	4-35/100[24]	1/1	1/110
Pyloric Stenosis				
White	1/790[5]	0/329[7a]	3/33	3/110
Black	1/2100[5]	—	—	—
Atrophy-Small Intestine	Not Known (Rare)	—	1/1	1/110
Meckel's	15/1000[24]	—	—	1/110
Duplications	Not Known (Rare)	None Reported	0/10	0/110

autopsy data. No prospective studies for gastrointestinal malformations in D.S. have been reported. Table 2 shows a list of other minor gastrointestinal or genito-urinary malformations which have been described in patients with D.S.

University of Minnesota Hospitals Cases (1963-1968)

Cases seen at the University of Minnesota Hospitals with the diagnosis of D.S. from 1963 through 1968 numbered 110 patients (Tables 1 and 3). Fourteen cases (12%) had GI malformations. T. E. fistulae occurred in one patient and was the only D.S. in 16 patients with T. E. fistulae seen during the same period of time. Three cases of pyloric stenosis occurred in our series of D.S. for an incidence of 2.7% and represented 9% (3/33) of the total pyloric stenosis patients seen during the same period of time. Duodenal atresia occurred in two patients for an incidence of 1.8%. This represents 33% (two of six) of the patients seen with duodenal atresia. Annular pancreas was seen in one patient and represented the only patient seen with this condition during this five year period. One D.S. patient was seen with unremitting chronic diarrhea and malabsorption syndrome, who at autopsy, had atrophy of the small intestinal villi. No similar cases were seen during this five year period. Meckel's diverticulum is a rather common disorder, yet was present only in one patient with D.S. Two patients with D.S. had Hirschsprung's disease and represented 15% (two of 13) of the total patients seen with Hirschsprung's disease. Imperforate anus occurred in three patients and represented three of 11 patients (27%) seen with that condition. Diastasis recti was present in many patients but was not uniformly reported and therefore the incidence could not be determined. Approximately 40% of the present cases had an autopsy examination. Complete evaluation of the autopsy results are not know as some died at home or at another hospital.

Table 3 lists other associated anomalies of interest in the present series: five cases of cataracts; three with chronic persistent diarrhea with no evidence of malabsorption; two patients with lymphoma; one patient with medullary sponge kidney; one with lupus erythematosus; and twelve patients with chronic, persistent infections.

Congenital heart disease was present in 52 patients for an incidence of 47%. This correlates well with Rowe and Uchida's[2] figure of 40%. Fifty-nine percent of the cardiac cases in the present series had an AV canal. The fact that the University of Minnesota acts as a cardiac referral center may account for the slightly higher incidence of congenital heart disease in our series.

Comment

The initial patient who presented with pyloric stenosis is of interest for several reasons. Presentation at fourteen weeks is rare. Only six cases have been reported to develop after three months of age.[4,5,6,7B] None were associated with D.S. Three cases of pyloric stenosis with D.S. have been reported but clinic data related to the time of onset of symptoms is not available on these cases. In our patient, the upper GI series was done to demonstrate any abormal peristalsis and to judge the relative size of the lumen to the olive. The x-ray studies revealed there was decreased motility secondary to decreased force of the peristaltic waves which are normally quite forceful in typical cases of pyloric stenosis. This type of peristalsis has been seen by radiologists at the University of Minnesota Hospitals in children who have developed retardation for many reasons. The decreased force of gastric contractility may very well explain the delayed onset of symptoms in this patient.

TABLE 2
Other Conditions Reported to be Associated With Down's Syndrome

Condition:	Incidence per live birth
Hiatus Hernia[2]	Not Known
Cleft Lip[2]	1/500-1000
Cleft Palate[2]	1/750
Inguinal Hernia[2]	2-13/100
*Umbilical Hernia[2,24]	Depends on Age
Diaphragmatic Hernia[2]	Not Known
Exstrophy of Bladder[2,1]	1/30,000

*Increased incidence in Down's Syndrome reported in all above conditions.[24]

TABLE 3
Patients With Conditions Other Than GI Malformations in 110 Patients

Cataracts	5
Chronic Diarrhea	3
Lymphoma	2
Medullary Sponge Kidney	1
Chronic Infection	12
Lupus	1
Congenital Heart Disease	52
(AV Canal)	30

There has been reported a frequent association of pyloric stenosis in Long Arm "21" Syndrome (antimongolism).[25] Pyloric stenosis has been reported in association with Cerebro-Hepato-Renal Syndrome, Cornelia De Lange Syndrome, Smith-Lemili-Opitz Syndrome and 18 Trisomy Syndrome.[25]

Down's Syndrome (D.S.) and Tracheo-Esophageal Fistula (T.E.)

T. E. fistulae has been mentioned in association with D.S. in eight cases in the English literature.[2,3,23] Little clinical material is available to determine the types of fistulae and the clinical presentation in these cases.

Down's Syndrome and Duodenal Obstruction

In 1939 the association between D.S. and duodenal obstruction was observed.[2] A recent review revealed that 150 of 503 patients with congenital duodenal obstruction had D.S. (29%).[12] The incidence in the literature for duodenal obstruction in D.S. is about 26% [range 18-31%].[8,9,10,11,14,15] The vast majority of the duodenal obstructions in patients with D.S. are of the "intrinsic" variety. This fits well with the concept that in D.S. the bulk of observed pathology occurs because of development that is fundamentally different from normal. The reason for the aberrant development has not been entirely explained.

Patients with D.S. and duodenal obstruction had a significantly higher operative mortality (56%) than did those without D.S. operated on for duodenal obstruction (40%).[10,12]

Down's Syndrome and Hirschsprung's Disease (H.D.)

Hirschsprung's disease and its association with D.S. was first noted by Carter in 1958.[1] Since that time there have been twenty-four cases reported.[17,18] From nine studies of H.D., 2% of the patients with H.D. had associated D.S.[17] This differs from our findings in which 15% of patients with H.D. had associated D.S. In our series, 1.8% of patients with D.S. had H.D. In contrast to the H.D. patient that did not have D.S., the maternal age was advanced in all reported cases with associated D.S.[17]

Down's Syndrome and Imperforate Anus

Carter, in 1958,[1] reported two with D.S. and imperforate anus. Ten other patients are reported with D.S. and imperforate anus.[1,23] The three cases of imperforate anus and D.S. also had congenital heart disease. Recently another case of D.S. and imperforate anus was seen at the University of Minnesota Hospitals. This child did not have congenital heart disease but has a sibling with congenital pulmonic valvular stenosis.

Down's Syndrome and Annular Pancreas

Annular pancreas has an incidence in the general population of one in 10,000 to 40,000 live births.[24] D.S. occurred in 4-35% of these reported cases.[24] One of these cases also had Hirschsprung's disease and intestinal malrotation.[11]

Prognosis

In reviewing all gastrointestinal malformation, it becomes apparent that these are significant as causes of death in D.S., ranking only behind cardiac malformations and infections. They accounted for 8% of the total deaths in our series.

Etiology

It is also apparent that there is a great overlap between the various gastrointestinal malformations, and they often occur simultaneously in the same patient. The commonly cited etiological mechanism is that these malformations are caused either by defective canalization or vascular mechanisms with determination residency on chromosome 21. There is no direct evidence for this interpretation.

Recommendations

Because of the high incidence of gastrointestinal malformations in D.S., these should be carefully looked for in every newborn with this condition. It is recommended that a barium enema and a upper GI series with small bowel follow through be performed on all patients with D.S. The yield of pathology (12%) appears well worth the effort required. Conversely, careful attempts should be made to detect D.S. in all newborns with significant gastrointestinal abnormality since the diagnosis of D.S. is not always readily apparent in the newborn period.

Summary

One hundred and ten cases of D.S. were seen at the University of Minnesota Hospitals for 1963-1968. Fourteen patients had associated gastrointestinal malformations. Pyloric stenosis in association with D.S. has not been previously reported.

References 1-25 will be found on page 579.

Azulfidine Agranulocytosis with Bone Marrow

Megakaryocytosis, Histiocytosis and Plasmacytosis

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SALICYLAZOSULFAPYRIDINE *(Azulfidine®)*§ is widely used in the treatment of ulcerative colitis.[1,2,3] Common side effects include headache, nausea, vomiting, epigastric distress, arthralgia, skin eruptions and a mildly elevated temperature. Other reactions such as crystalluria,[1] paresthesia,[4] diarrhea,[5] thyroiditis and tracheolaryngitis with bronchospasm,[6] have been described. Hematologic reactions may include methemoglobinemia, sulfhemoglobinemia,[7,8] cyanosis not related to met- or sulfhemoglobinemias,[1] Heinz body anemia,[8-10] hemolytic anemia[8-11] and jaundice.[12]

Agranulocytosis as a toxic manifestation of this drug, although uncommon, is well established. Thirteen cases with this serious complication have appeared in the literature (Table2).[1,2,12-22] Three additional unpublished cases have been reported to the A.M.A. Registry on Adverse Drug Reactions.£

This paper describes the clinical course and recovery of a patient with Azulfidine® agranulocytosis. Unique cellular changes observed in serial bone marrow examinations are described. Clinical, laboratory and therapeutic findings are compared with other cases in the literature.

Case Report

A 67-year-old white male farmer with dermatomyositis controlled with prednisone (20 mg every other day), was hospitalized for ulcerative colitis. Azulfidine, 1 gram four times a day, was added to the prednisone regimen. This resulted in prompt symptomatic improvement. Hematologic parameters were normal. Four week after discharge and six weeks after starting Azulfidine® he was rehospitalized because of cough, malaise, fever, and roentgenographic evidence of pneumonia. Hematologic studies showed anemia and leukopenia (white blood count, 550/mm³). The differential count was 97% lymphocytes and 3% monocytes. Blood cultures grew out E. coli. Azulfidine® was stopped, prednisone continued and the infection treated with penicillin, streptomycin and kanamycin. (See clinical course Figures 1 and 2.)

Table 1 details the sequential bone marrow changes following discontinuance of Azulfidine®. On the third hospital day the marrow was hypercellular and granulocytic elements were absent. Normoblasts were decreased and plasma cells, lymphocytes, histiocytes and megakaryocytes were strikingly increased. Three units of whole fresh blood were given because of anemia. A marked proliferation of immature granulocytes was present by the 10th day giving the appearance of a maturation arrest. On the 14th day these granulocytes were in various stages of maturity. This was followed by a return of granulocytes and reticulocytes to the blood. Subsequent bone marrows 28 and 115 days later were normal. During the period of agranulocytosis platelets remained slightly increased in numbers in the blood and plasma cells comprised up to 15% of the differential.

Using the leukocyte agglutinin method of Payne,[23] the patients serum on the ninth day contained antibodies which agglutinated leukocytes of two out of 10 normal compatible subjects. Similar studies 17 months later, with or without Azulfidine® in the test system, were negative.

TABLE 1
Bone Marrow Differential (1 000 cells counted.)[40]

Bone Marrow Differential (1,000 cells countad) (40)

Oays after drug stoppad	3	7	10	14	28
Normoblasts %	10.2	9.9	17.7	10.2	19.9
Myeloblasts %	1.5	2.7	1.1	0.3	0.5
PMN and precursors %	0.0	15.6	68.4	84.4	70.5
Eosinophiles and precursors %	0.0	0.5	0.4	0.0	2.5
Basophiles and precursors %	0.0	1.4	0.7	0.4	0.2
Lymphocytes %	37.0	26.4	4.7	3.1	4.8
Monocytes %	0.5	3.9	3.5	1.1	1.6
Plasma cells %	54.7	39.6	3.5	0.5	0.5
Histiocytes	††	††	†	+	±
Megakaryocytes	††	††	††	↓	N
B.M. cellularity	++	++	++	+++	N
B.M. iron stores	††	††	††	††	N
M:E volume %	4.0	2.5	10.0	12.0	4.5
Fat and P.V. layers %	3.0	2.0	4.0	trace	2.0

‡ or † or †† = decreased or increased or markedly increased.
+++ or ++ or + ± = markedly hypercellular or hypercellular or present or occasionally present.
N = normal.
M:E = myeloid:erythroid.
B.M. = bone marrow.

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§Pharmacia Laboratories, Inc., New Jersey.

£A.M.A. Registry on Adverse Drug Reactions: Personal communication, Feb. 4, 1970.

Discussion

Absorption and Distribution

Salicylazosulfapyridine is a poorly absorbed sulfonamide composed of salicylic acid and sulfapyridine linked together by a diazo bond. When taken orally the drug is partially absorbed. A portion is excreted unchanged through the kidneys. The remainder is deposited in the connective tissue of the intestines where it is broken down to aminosalicylic acid and sulfapyridine. Although the mode of action of the drug is unknown, it is assumed that its therapeutic effect takes place in connective tissue.[1-3]

Pathogenesis of Agranulocytosis

The pathogenesis of drug-induced agranulocytosis is not clearly understood. Its low incidence suggests an idiosyncrasy in susceptible individuals. Various possibilities include interference with cellular metabolism, immune mechanisms, and suppression of production or inactivation of hematopoietic factor(s). The latter hypothesis remains a speculation.[33]

Interference with cell metabolism

The first hypothesis has been supported by studies of chlorpromazine-induced agranulocytosis, where interference of cellular metabolism has been demonstrated. In the presence of chlorpromazine, bone marrow incorporation of radio-labeled thymidine and uridine into the granulocytic series is defective.[24,25] These findings are not unique, however, since marrow incubation studies in 75% of random hospital patients also show defective incorporation. Similar studies have not been reported for Azulfidine®.

Immune Reaction

Immune mechanisms for drug related agranulocytosis have been demonstrated for some drugs.[18,26-30] Bone marrow aplasia on an immune

TABLE 2

Summary of Azulfidine® Agranulocytosis Cases from the Literature.

Cases Reported	Svartz* (1) 1942	Swartz 1942	Nja 1945	Levy 1949	Koskinen 1954	Evans 1958	After trial with 2nd dose	Roth 1959	Ritz 1960	Vinggard 1962	Thirkettle 1963 Case #1	Thirkettle 1963 Case #2	Panitz 1963	Darling 1965	Present Case 1970
Age in Years	—	45	9½	68	22	35		52	58	64	60	69	39	64	67
Sex	—	M	M	F	M	M		M	M	F	M	M	M	F	M
Daily dose in gm	—	4 then 3	4	4	4	4	1 then 2	4	4 then 3	3	3	3	8	2	4
Duration of therapy in days	27	15	12	31	2½	49	9	46	34	30	58	19	39	31	42
Days after drug stopped to first bone marrow	—	—	3	4	9	7	1	5	1	unsuccessful	1½	3	?	9	3
Bone marrow cellularity	—	—	↓	↓	↓	↑	↓	Active	↓	—	A G	A G	↑	A G	↑
Normoblasts %	—	—	↓	42	↓	21.6	58.0	Active	1	—	R	R	1	R	10.2
Granulocytes and precursors %	—	—	—	14	1	73.9	28.4	Present	0	—	A S U	A N U	—	A N U	1.5
Lymphocytes %	—	—	—	33.5	↓	4.4	13.1	—	↑	—	L	L	—	L	37
Monocytes %	—	—	—	20.0	—	0	0	—	—	—	O C	O C	—	O C	0.5
Plasma cells %	—	—	—	3.5	—	0	0.3	—	↑	—	Y	Y	—	Y	54.7
Reticulum cells %	—	—	—	1	—	—	—	—	—	—	T O	T O	—	T O	—
Histiocytes %	—	—	—	—	—	—	—	—	—	—	S	S	—	S	††
Megakaryocytes %	—	—	—	1	—	0.1	0.2	—	1	—	I S	I S	—	I S	††
Unclassified cells %	—	—	—	3	—	—	—	—	—	—	—	—	—	—	—
Complications	Fever	Rash	—	Staph. Septicemia	Fever, Septic condition	Rash	—	Rash E.coli Septicemia	Rash	Stomatitis, Necrotizing Pharyngitis, E.coli Septicemia, Pneumonia	Rash Pseudomonas Septicemia	Rash E.coli Septicemia	Purulent Pharyngitis	Fever Stomatitis	E.coli Septicemia Pneumonia
Therapy	—	—	—	Penicillin	Chloromycetin, Terramycin, Penicillin, Streptomycin, Cortisone	—	—	—	Penicillin, Streptomycin, Chloramphenicol, Madribon	Penicillin, Streptomycin, Chloramphenicol, Madribon	—	—	Penicillin	Chloromycetin, Erythromycetin	Penicillin, Streptomycin, Kanamycin Prednisone
Outcome	Expired	Recovered	Recovered	Recovered	Recovered	Recovered		Expired	Recovered	Expired	Expired	Expired	Recovered	Recovered	Recovered

* Case mentioned only in discussion.

↓ or ↑ or †† Decreased or Increased or Markedly Increased.

— Not reported.

basis has been produced in experimental animals.[32] It has been suspected that certain drugs, including Azulfidine® act as haptens which are capable of combining with leukocyte constituents. This stimulates the production of antibodies directed against these same cells and in some cases the antibodies may react with leukocytes from individuals with compatible ABO and Rh blood factors. The leukocyte agglutinins found in our patient were obtained six days after blood transfusion. Repeat studies 17 months later were negative. There are a variety of possibilities to explain the presence of these weakly positive leukocyte agglutinins. These include: post-transfusion isoantibodies,[34-36] antibodies in transfused blood, and antibodies related to the patients collagen disease[37] and/or Azulfidine®.[18]

Blood, Bone Marrow and Leukemoid Reactions

The usual picture of a drug-induced agranulocytosis in its early stages is that of leukopenia with a hypocellular or, less commonly, a normocellular bone marow. Coupled with the leukopenia is an absolute reduction in numbers of granulocytes, monocytes and lymphocytes. The differential blood count shows a relative lymphocytosis, often 100%. Marrow elements are predominantly lymphocytes. The granulocytic series is markedly decreased or absent. The erythroid element of the marrow is slightly to moderately decreased, but may appear normal or increased because of the paucity of other cellular elements. Megakaryocytes are usually decreased and plasma cells are normal or decreased.

In contrast, the unusual hypercellularity of the bone marrow in our patient (Table 1) was due to marked increases in histiocytes, megakaryocytes, and plasma cells. The return of granulocytic cells to the bone marrow was followed by an intense neutrophilic leukocytosis and a marked absolute monocytosis in the blood. Leukocytosis in the recovery phase of drug induced agranulocytosis may be so intense, as it was in this case, that a leukemoid or leukoerythroblastotic picture is seen. This type of response, in addition to hyperplasia of granulocytic marrow elements, may be misinterpreted as a myeloproliferative disorder, leukemia,[38] or maturation arrest. With observation it will be appreciated that such patterns represent different periods of marrow recovery.[25]

Two additional unusual findings in this case were a peak lymphocytosis in the blood, which followed those of neutrophils and monocytes, and a plasmacytosis (15%). The lymphocyte pattern confirms Nja's observations in a case of Azulfidine® agranulocytosis. This is in contrast to the cell recovery pattern for chlorpromazine agranulocytosis.[25] The reason and significance of the delay in peak lymphocytosis is unclear. The plasmacytosis suggests the possibility that alterations in immune mechanisms may have occurred in this patient.

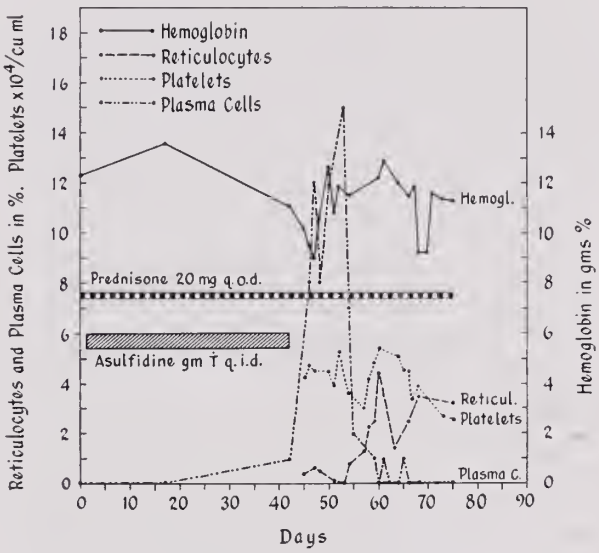


Fig. 1—Clinical Course—Hematology Data.

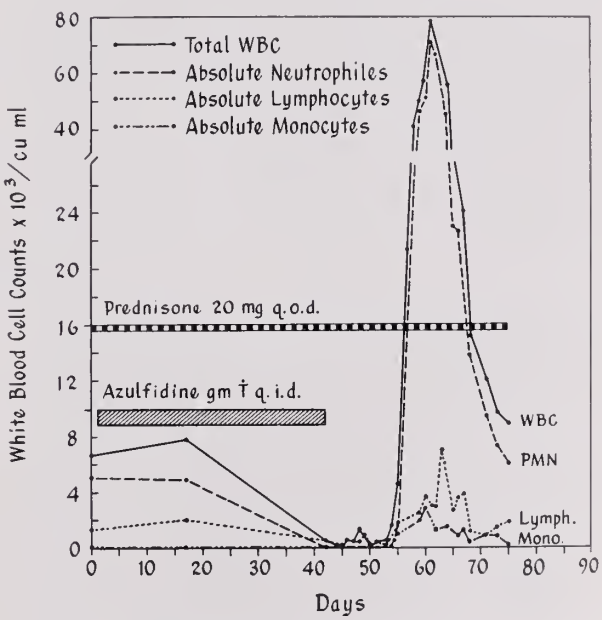


Fig. 2—Clinical Course—Hematology Data.

The increased numbers of histiocytes in the marrow may be the result of stimuli to clear the marrow of damaged cells. However, the increased numbers of megakaryocytes in the marrow, in addition to the histiocytosis, appears to be unique. No other reported case of Azulfidine® agranulocytosis showed similar features (Table 2.)[1,2,12-22] Additional sequential studies of blood and bone marrow in other cases will be needed in order to assess the significance of these findings.

Recognition and Therapy

Patients receiving drugs potentially toxic to the bone marrow should have regular blood studies including blood smear examinations and white blood counts. Fortunately, Azulfidine® agranulocytosis appears to be infrequent. In the event of fever, rash, "colds", sore throat or any unusual symptomatology patients should be instructed to stop drugs immediately, and contact their physician. If the blood and bone marrow findings are similar to those previously described, Azulfidine® should be discontinued and therapy directed toward combating infection.

Steroid Therapy

The use of corticosteroids in addition to antibiotics and blood transfusions, has been advocated by some,[39,41] however, this is controversial.[31,42] Our patient, Koskinen's, Ritz's and two of the three unpublished cases reported to the A.M.A. Registry on Adverse Drug Reactions received corticosteroids and all recovered. Only six of the remaining 12 patients (Table 2) who were not on sytemic corticosteroids recovered. This data does not establish the role of steroids in treating such patients, but it does emphasize the need for further information. Other types of steroids, such as anabolic steroids, have been effective in some types of drug-induced bone marrow aplasia.[45,46] None of the reported cases of Azulfidine® agranulocytosis have been treated with this class of steroids.

Antibiotics

Antibiotics play an important role in increasing survival. In the pre-antibiotic era the mortality of drug-induced agranulcytosis was as high as 80%.[41] Despite appropriate supportive measures and the use of appropriate antibiotics, mortality still remains high (5 to 50%).[41,43,44]

Summary

The course of a patient with Azulfidine®-induced agranulocytosis is described. Serial bone marrow studies during the period of agranulocytosis and recovery phase showed the unusual findings of hypercellularity with a marked increase in megakaryocytes, histiocytes and plasmacytes. The circulating blood showed plasmacytosis. This combination of blood and marrow findings have not been previously described. Upon recovery, the bone marrow and circulating blood were completely normal. Steroids may have contributed to the patient's survival. All patients reported (5), including the present case, who received steroids recovered.

Acknowledgements

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11-46. May be found on page 600.

Acute Acalculous Cholecystitis

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Cholelithiasis is found in 90 to 95 per cent of patients with acute cholecystitis and is believed to be a major etiologic factor. Little attention, however, has been directed to those cases where acute cholecystitis occurs in the absence of stones. We review here all cases of acute acalculous cholecystitis occurring at the University of Minnesota and allied hospitals during a 16-year period 1954 through 1969.

Chart Review

In the years 1954 through 1969 780 patients underwent cholecystectomy for acute cholecystitis at the University of Minnesota Hospitals and affiliated teaching hospitals. In each instance the diagnosis was confirmed by pathologic examination. No calculi were found in 34 (4.4 per cent) specimens. The patients' ages ranged from 18 to 87 years (average 57).

Medical History

Only four patients had symptoms suggestive of gallbladder disease, fatty food intolerance. Eight patients developed acute acalculous cholecystitis while recovering from operative procedures, only two of which were intra-abdominal. Four others had suffered extensive trauma in automobile accidents, and two of these had operations related to the injuries.

Four other patients were alcoholics, and one of these developed cholecystitis while being treated for bleeding esophageal varices. Nine patients had been treated for cancer including lung, stomach, prostate, thyroid, cervix, breast and testis. Other associated medical problems included ulcerative colitis, heart disease, arteriosclerotic peripheral vascular disease, and gastric ulcer.

Symptoms and Signs

Right upper quadrant pain was the most common complaint, noted in 26 of the 34 case records. In two the pain was diffuse throughout the abdomen and in one it was periumbilical. Three patients had no pain and one patient was comatose.

Right upper quadrant tenderness was detected in 28 patients. Two had diffuse abdominal tenderness and three had none. Twenty-two patients vomited. Six of the 34 had a palpable right upper quadrant mass. Abdominal distension was present in 12, bowel sounds were decreased or absent in 14, and clinical jaundice was detected in seven instances. Twenty-seven patients had fever.

Laboratory Studies

The white blood cell count ranged from 4750 to 29,000 cell per cu mm, exceeding 10,000 in 23 instances. The serum bilirubin was measured in 25 patients and was elevated in 12, exceeding 3 mg/100 ml in seven. The serum glutamic oxalic transaminase was elevated in six of 10 measurements, and the alkaline phosphatase was increased in eight of 18 patients.

Roentgenographic Studies

Biliary x-ray studies were done in 12 patients. The gallbladder did not visualize in 11 examinations. Air was seen in the gallbladder lumen in one.

Preoperative Diagnosis and Operation Performed

There was a delay of one to 67 days from the onset of symptoms to operation. Acute cholecystitis was not suspected in 12 instances. Incorrect diagnoses included subhepatic abscess, hepatic abscess acute appendicitis, "inflammatory mass", ruptured spleen, and mesenteric vein thrombosis.

Cholecystectomy was performed in all cases, although cholecystostomy was done initially in three instances because inflammatory reaction obscured the anatomy. Elective cholecystectomy was performed one to two months later. Common bile duct exploration was carried out in four patients because of jaundice. Common duct

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exploration was not performed in three jaundiced patients, one of whom had a normal operative cholangiogram.

Pathology and Bacteriology

Acute cholecystitis was confirmed histologically in all cases of acalculous cholecystitis. The gallbladder wall showed areas of gangrene in 14 specimens. There were three instances of empyema and three of localized perforation.

The bile was cultured from 17 patients and the surrounding peritoneal fluid from eight. Eight of the 25 specimens were sterile. *Escherichia coli,* the most common organism, was cultured eight times. Other organisms included alpha hemolytic streptococcus, coagulase negative staphylococcus, klebsiella, aerobacter, pseudomonas, clostridium, and bacteroides. In three instances the organism found in the bile had previously been cultured from the blood. One patient had a urinary tract infection caused by the same organism found in the bile.

Morbidity and Mortality

There were seven deaths. Two occurred in patients who had been involved in automobile accidents and had extensive injuries. Cholecystitis developed five and 35 days after injury. A 20-year old man was brought to the University of Minnesota Hospitals five days after treatment in another hospital for injuries sustained in an automobile accident. He was comatose and was operated upon because blood was found in the peritoneal aspirate. He died in the early postoperative period with pneumothorax and adrenal hemorrhage. A 66-year old woman died of congestive heart failure one month following cholecystectomy, vagotomy and gastrectomy.

Three deaths occurred in patients who developed acute cholecystitis while recovering from other surgical procedures. A 63-year old man who had the onset of symptoms 20 days after insertion of an aortic valve prosthesis died of cardiac arrest shortly after cholecystectomy. A 79-year old woman developed pneumonia after radium insertion for carcinoma of the cervix. She developed cholecystitis 27 days later and died of continuing pneumonia and septicemia one month following cholecystectomy. The third patient was a 73-year old man who had gram negative sepsis and cholecystitis following thyroidectomy and radiation for lymphoblastoma of the thyroid. A bleeding dyscrasia developed after cholecystectomy, and death resulted from gram negative sepsis.

Two other patients, both alcoholic, also succumbed. One had cholecystectomy for acute cholecystitis discovered during emergency portacaval shunt. He died 15 days postoperatively of recurrent upper gastrointestinal hemorrhage and hepatic coma. An 85-year old male developed congestive heart failure following cholecystectomy and died.

Three non-fatal complications related to cholecystectomy. Two patients had prolonged bile drainage which ceased spontaneously. A 78-year old man developed hepatitis six months following cholecystectomy, was treated medically and recovered.

Incidence

In large series of acute cholecystitis 90 to 95 per cent of the patients have gallbladder stones and two-thirds are women.[2,6,8] Conversely, three-fourths of the patients with acalculous cholecystitis are male. In the present series also, when six male patients from the Veterans Administration Hospital are excluded, 71 per cent of the patients were male. The incidence of the acalculous variant is significantly higher when cholecystitis occurs in the postoperative period [10,12], after trauma[11], or in children.[3,7]

Pathogenesis

Experimental work indicates that bile stasis, impairment of blood supply, and cystic duct obstruction are the most important factors in the development of acute cholecystitis.[13]

Infection has also been proposed as a cause of cholecystitis. Lindberg et al.[11] found infected bile in nine of 12 wounded soldiers with acute acalculous cholecystitis. Six of the nine had wounds infected by the same organism subsequently found in the bile. Cole et al.[4] have proposed that infection is a late event imposed upon an already inflammed gallbladder. A lower incidence of positive cultures of bile and gallbladder wall is found if the specimen is obtained in the early, rather than late, phase of acute cholecystitis.[1,8]

Reflux of pancreatic secretions into the gallbladder has also been implicated in the etiology of cholecystitis. Colp et al[5] found amylase and trypsin in the bile of inflammed gallbladders and Wolfer[14] produced cholecystitis by injecting

pancreatic juice into the gallbladder of dogs.

Clearly, no single explanation can account for all cases of acute acalculous cholecystitis. Most of our patients were being treated for other illnesses at the time of onset of acute cholecystitis. Eight developed cholecystitis while recovering from operations and four following extensive injuries. Several previous reports have implicated surgery and trauma as predisposing to acute acalculous cholecystitis.[10-12]

Many of our patients had arteriosclerosis. Their gallbladder blood flow may have been decreased to a level where further minor insults could lead to cholecystitis. No cystic duct obstruction was evident in these patients.

Summary

Thirty-three patients developed acute cholecystitis without gallbladder stones. There were 25 males and eight females. Three-fourths were older than 50 years. Only four patients had prior symptoms referable to the biliary tract. Eight developed acute cholecystitis while recovering from surgery, and four had suffered extensive trauma.

Their symptoms did not differ appreciably from patients with acute acalculous cholecystitis. Right upper pain and tenderness, vomiting, abdominal distention, decreased bowel sounds, jaundice, and fever were frequent.

Fourteen specimens showed gangrene. There were three instances of empyema and three of localized perforation. Seventeen of 25 specimens were infected; *E. coli* was the most common organism.

We believe that decreased gallbladder perfusion caused by arteriosclerosis possibly combined with a low cardiac output contributed to the development of cholecystitis. It is not clear if cystic duct occlusion was a factor.

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Now when a doctor's patients are perplexed,
A consultation comes in order next—
You know what that is? In a certain place
Meet certain doctors to discuss a case
And other matters, such as weather, crops,
Potatoes, pumpkins, lager-beer, and hops.*

*Oliver Wendell Holmes, Sr.: Rip Van Winkle, M.D., 1870.

Anorexia Nervosa

94-Year-Old Woman Treated with Electroshock

IRVING C. BERNSTEIN, M.D.*

ANOREXIA NERVOSA is a serious nervous condition in which the patient loses his appetite and systematically takes but little food, so that he becomes greatly emaciated."[1] When this illness endangers life, treatment modalities should be utilized which are effective in the shortest period of time.

Electroshock should be used to treat the affective components of severe psychiatric illnesses, whether they be neurotic depressions, psychotic depressions, schizophrenic reactions, or manic depressive reactions. It is also effective for psychoneurotic symptoms such as pain and anorexia which are indicative of severe affective states.[2] Anorexia Nervosa in young women has been treated successfully with electroshock,[3] but its use need not be limited to youthful patients with this illness.

*Clinical Professor of Psychiatry, and Obstetrics and Gynecology at the University of Minnesota, and Chief of Psychiatry at Mount Sinai Hospital in Minneapolis.

Case Report

A 94-year-old widow was admitted to Mount Sinai Hospital on May 22, 1971 after she had fallen to the floor and sustained an injury to her left hip. The orthopedist who saw her diagnosed her as "mentally disturbed and having a fracture in the intertrochanteric area of the left femur." This fracture was successfully operated upon on May 26, 1971. On May 27, 1971 she refused to eat and was noted to be uncooperative, agitated, depressed, and paranoid. This refusal to take anything by mouth continued, and she became progressively weaker. The doctors and hospital personnel involved in caring for her became concerned because she was obviously going to



Figure—Ninety-four-year-old widow treated for anorexia nervosa. (Permission given by daughter to use picture.)

starve herself to death.

Her only living relative, a daughter, was extremely distraught, especially about her mother's not eating, and had ambivalent feelings about permitting her mother to die. She said: "Mother has tried to control me all my life by making me feel guilty about not taking care of her, but she did get me out of Russia after World War I. Still, she's been sick so long she might as well die."

The patient's condition continued to deteriorate and on June 8, 1971 a psychiatrist was called in for consultation. He commented: "This lady has been schizophrenic for years, is now almost catatonic, and should be treated with electroshock immediately." With much reluctance, the daughter gave permission for electroshock therapy. Her attending physicians were not enthusiastic about this recommendation and decided to institute intravenous feedings instead. The patient's weight at this time was 80 pounds. With this conservative management, the patient's hydration improved somewhat, but she continued to starve herself. She was completely uncooperative and rebellious. Finally, on June 21, 1971, her doctors agreed the patient would not improve on conservative management and consented to the administration of electroshock. The first treatment was given the same day. After the second treatment on June 23, the patient began to eat and her general condition and attitude began to improve. Electroshock was discontinued after the fifth treatment on June 30, only nine days after it had been instituted, because of the patient's dramatic improvement, including a weight gain of six pounds. She was very cooperative, ate well, and showed almost no paranoid thinking. At this time, her daughter stated the patient was better than she had been for over 50 years and remarked sorrowfully that electroshock had been considered for her mother's schizophrenia 15 years earlier, but was not given because "the patient is too old." The patient continued to improve and was discharged to a home for the aged on July 12, 1971, when a bed first became available.

Discussion

This patient, despite her age, can be considered a case of anorexia nervosa. She demonstrated the typical psychodynamics that Frazier[4] describes. "These emaciated patients suffering from lack of affection and severe emotional isolation utilize the pursuit of thinness as a weapon in the struggle for control of family members." In addition, this case corroborates Kalinowsky's statement[5] that electroshock is more effective than neuroleptic drugs in many schizophrenic syndromes.

Summary

A case of anorexia nervosa has been presented to demonstrate the effectiveness of electroshock therapy in this entity and to emphasize that advanced age is no contraindication for its use.

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Cover Photograph

"Tumbler Landscape"

The cover photo was taken two years ago by Dr. Donald C. Bell, internist, at Snowmass, Colorado. He and his family were at lunch and the empty tumbler on the table cast this unusual reflection. Dr. Bell thought this would create an interesting picture and took the cover photograph.

Dr. Bell practices at the Fairview Hospital and the Metropolitan Medical Center in Minneapolis, Minnesota.

Meeting

The 32nd Annual AMA Congress on Occupational Health will be held at The Drake Hotel in Chicago, September 11-12, 1972. Contact Dr. Henry F. Howe, AMA, 535 North Dearborn Street, Chicago for further information and reservations.

Case Report-

Megaloblastic Anemia and Oral Contraceptives

W. M. SALTER, M.D.*

ORAL CONTRACEPTIVES have become implicated in an ever increasing number of serious side effects.[1-3] Streiff[4] reported seven cases of megaloblastic anemia associated with the use of oral contraceptive agents. Others have similarly associated the use of oral contraceptive and folate deficiency.[5] This report concerns a severe megaloblastic anemia apparently due to long term cyclic administration of an oral contraceptive.

Case Report

A 47-year-old white female was hospitalized for weakness, lethargy and dyspnea on exertion progressively and gradually more severe over a four month interval. She had six previous pregnancies, the youngest child five years of age. She denied weight loss, sweats, fever or chills and had no diarrhea, change in character of stools, nausea or vomiting. Specifically she denied symptoms suggesting malabsorption problems, i.e. frothy foul stools fatty or oily appearing bowel movements. There was no numbness, tingling of hands or feet and no complaint of sore tongue. She had a past history of probable discoid lupus some fifteen years earlier. The patient's medications were only Ovulen-21 (ethynodioldiacetate and mestranol) and intermittent diuril (chlorothiazide) for mild dependent edema. She had taken Ovulen-21 on a 20-day cycle, five days off, continuously for over four years. She had no other past illnesses. Her diet had been well balanced with no peculiar dietary habits.

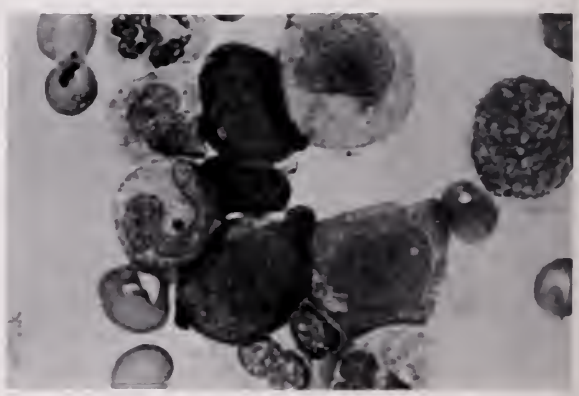
Physical examination found a pale-appearing but well nourished female. Her weight was 116 pounds. The tongue was pale and smooth. A grade 2/6 stystolic murmur was present at the left sternal border of the heart. The blood pressure was 120/76. The abdomen was normal. The liver and spleen were not palpable. There were no masses. The pelvic and rectal exams were also normal. There were small purpuric areas over both forearms and trace of edema of both lower legs. The reflexes were active and equal. The vibratory and position sense were intact. Coordination and muscle strength were also normal.

Laboratory Findings

Initial hemoglobin was 4.7 gm%, hematocrit 14%. RBC 1.4 million per cmm. The mean corpuscular volume was 147 cubic micra. The white blood count was 4,700 with 75% segmented neutrophils, 1% stabs, 23% lymphocytes and 1% eosinophils. The platelet count was 98,000. The peripheral blood smear showed prominent macrocytosis with some ovalocytes but only a mild anisopoikilocytosis. There were numerous hypersegmented neutrophils. A bone marrow aspiration revealed a myeloid erythroid ratio of 2:1 with erythropoiesis being megaloblastic (see Figure). Giant and hypersegmented neutrophils were present. The reticulocyte percentage was 0.2%. A serum iron was 270 micro gm% and the iron binding capacity 270 micro gm%. A gastric analysis revealed 55 millequivalents of free acid after 50 mgs. of histalog intramuscularly. The transaminase was 54 units, the lactic dehydrogenase 4700 units, and the serum bilirubin was 0.3 mg% total and 0.15 mg% direct. The total protein was 5.0 gm% with 3.4 gm% albumin. The BUN was 8 mg%, the cholesterol 145 mg%, and the alkaline phosphatase 53 international units. The fluorescent antinuclear antibody and L.E. preps were negative. A protein bound iodine was 6.4 mcg%. An eight-hour plasma B-12 absorption was calculated at 0.316% with normal values being greater than 0.2% absorption of administered dose of radioactive B-12. The serum B-12 was 140 picograms per ml‡ and serum folate was under 2 millimicrograms per ml†. The normal value of serum B-12 for females is 90-630 picograms and for folate, 5-21 millimicrograms per ml. A chest Xray and an upper GI with small bowel follow through studies were normal.

Hospital Course

Following completion of laboratory studies the patient was given 2 units of packed cells which brought the hemoglobin level to 8.4 gm%. The Ovulen-21 was withheld and folic acid 5 milligrams daily administered. Ten days following daily administration of folic acid



Figure—Bone Marrow Aspiration. Note megaloblastic changes and giant neutrophils.

*Internist, Willmar Medical Center, Willmar, Minnesota.

‡Both determinations performed by Bioscience Laboratories of Van Nuys, California.

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the hemoglobin was 9.3 gm% and the reticulocyte count 4.0%. On the 16th day after beginning folic acid therapy the hemoglobin was 10.9 gm%, the hematocrit 32%, the white blood count 9,250 and the platelet count 451,000. Four weeks after initiating therapy the hemoglobin rose to 13.9 gm% and hematocrit 41%.

Comment

The diagnosis and management of megaloblastic anemias, formerly a straightforward problem, has been complicated in recent years with the use of diverse drugs singly and in combination. It is known that hydantoin derivatives and some barbituates may interfere in folate absorption and p-aminosalicylic acid and colchicine with B-12 absorption.[6,7] Streiff[4] recently described seven women with folate deficiency and anemia with no explanation other than the fact that all were taking oral contraceptives regularly for at least 1½ years. In his studies Streiff noted that oral contraceptives blocked the absorption of dietary folate (polyglutamic folate) but not folic acid as found in vitamin preparations (monoglutamic folate). He noted that polyglutamic folate must undergo enzymatic change before absorption takes place. Results on 18 normal female volunteers demonstrated that oral contraceptives caused a mean reduction in food folate absorption by approximately 50%. In view of such findings the rarity of anemia is not well explained except to say that the usual American diet contains considerably more folate than the minimum required by an adult. Also, restoration of folate levels may occur in most women during the five day cycle free of taking these drugs.[4] It should be pointed out that it is not necessary to discontinue oral contraceptives when they are implicated as the cause of megaloblastic anemia but folic acid supplementation is necessary.

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Minnesota Medicine Cover Award, 1971



Louis A. Buie, Sr., M.D.

Sir Winston Churchill took up painting at age 40. Dr. Louis Buie, of the Emeritus Staff of the Mayo Foundation, waited until he was well past 70, and started then only because, during an illness, "my wife encouraged me to try." So energetically did he follow her advice that the Buie recreation room turned studio now hardly holds all his canvases. "I could always sketch." This talent is evident in charcoal heads of persons for whom he has high regard. With oils he paints "things I remember," and his memory is long, extending back to scenes of his South Carolina youth.

Dr. Buie is a world-famous proctologist and one of the first in his specialty. He practiced with the Mayo Brothers in Rochester.

The April, 1971, issue of MINNESOTA MEDICINE on which Dr. Louis A. Buie's painting "South Carolina, Remembered" is featured has been selected as the outstanding cover for 1971.

Letter to the Editor

Dear Editor:

This communication is prompted by my encountering an infant of seven months at a Crippled Children's Clinic on April 5th whose mother had been told by a Minnesota physician to begin the elimination of milk from her child's diet because it was bad for babies and children. The physician may have been misquoted, on the other hand, the mother was reducing the infant's milk under that understanding.

There seemed to be three reasons why the milk might be eliminated from the child's diet. The first is an allergic one which this child did not have. The second is an intolerance due to low lactose intolerance which this child did not seem to have either. Finally, the possibility that the fats of milk contribute ultimately to coronary problems. Since milk forms the essential part of an infant's diet throughout the first year at least, it would seem that eliminating it on this basis at the age of six months might be detrimental to the child's health. Ultimately, we may find that American children are given milk for too long a period of time and perhaps in too large quantities. At the present time despite the recent pronouncements about this by some in the field of cardiology, I question that the evidence is sufficiently sound to warrant tampering with the milk intake of infants below the age of one year. I refer your readers to a statement* put out by the Protein Advisory Group of the United Nations System concerning lactose intolerance. This Protein Advisory Group is made up of some very knowledgeable people in the field of childhood nutrition from all over the world. It is headed by Professor Bo Vahlquist who is director of the Department of Pediatrics in Uppsala, Sweden.

G. B. Logan, M.D.†
Rochester, Minnesota

*Copies may be obtained without charge from the Protein Advisory Group of the United Nations System, United Nations, New York 10017, U.S.A.

†Pediatrics, Allergy and Clinical Immunology, Mayo Clinic.

Dear Editor:

This is an addition to the letter that I wrote to you a short time ago regarding an apparent misunderstanding by at least one doctor and perhaps others in Minnesota about the need to restrict milk intake in babies. The initial letter concerned only lactose intolerance.

I should have included references to two articles in the February issue of *Pediatrics* for 1972. These articles concern the relationship between milk ingestion and atherosclerosis which is the concern of some cardiologists.

The first of the articles is a report from the Subcommittee on Atherosclerosis Council of Rheumatic Fever and Congenital Heart Disease of the American Heart Association. The second is a report of the Committee on Nutrition of the American Academy of Pediatrics. I will add only one quote from the latter report which summarizes the recommendation at the present time: "The Committee stresses that such dietary intervention is at present experimental and recommends against dietary changes for all children". The Academy of Pediatric Committee on Nutrition goes on to state that dietary intervention may be warranted in special circumstances but not before the children are one year of age.

George B. Logan, M.D.



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Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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Indication—Enovid-E is indicated for oral contraception.

The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

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Where "The Pill" Began

Editorials

Medical Writing Awards: 1971

"Who can confidently say what ignites a certain combination of words, causing them to explode in the mind?" E. B. White, Elements of Style

Who indeed?

Certainly not I.

Nevertheless I shall try to guess why the Board of Editors picked the following three articles as the best published in MINNESOTA MEDICINE in 1971:

Bring Back the Mustard Plaster, December, 1971, Seymour Handler, North Memorial Hospital, Minneapolis.

Splenic Rupture: A Review of 114 Cases, March, 1971, Dean B. Pratt, Robert C. Andersen, and Claude R. Hitchcock, Hennepin County General Hospital, Minneapolis.

A Physician by the Name of Ohiyesa, July, 1971, Thomas W. Milroy, Student Health Service, University of Minnesota, Minneapolis.

Why did the Board blow their minds over these three?

No one can say for sure.

Titles

But I think the three titles had a great deal to do with winning.

Take, for example, "Bring Back the Mustard Plaster." Now there's a title with flair. And mystery. It's got enough of both to lure the reader to find out who's plastering whom.

At first blush, you might not consider "Splenic Rupture: A Review of 114 Cases" as a title with much clout. You'd be wrong. It has clout for a couple of reasons—some obvious, others not so obvious.

In the first place, 114 cases with ruptured spleens are a lot of cases. The reader can only surmise that these authors must know what they're 'alking about. This is obvious enough. What's not so obvious is the importance of the authors' credentials and the readers' natural interest.

When you read a title, you consider the source. Hennepin County General Hospital has a national reputation for treating domestic casualties. This then is an article you must respect. Besides, ruptured spleens is a subject that would naturally interest many practicing physicians. After all, anytime the physician treats an accident victim with abdominal injuries, the thought of a bleeding gaping spleen flits through his mind.

Why "A Physician by the Name of Ohiyesa" has appeal is hard to explain. But the appeal is there. It's mostly an esthetic matter. The title just has lyrical charm—the right ring. Perhaps it's the Indian name of "Ohiyesa." Somehow that stirs the soul.

Something to Say

There's more, of course, to writing an award winner than picking a title.

In fact, there are three things, the title being one of them. John Shaw Billings (1838-1913), a physician who started the *Index Medicus,* defines these three as well as anyone:

> "First have something to say,
> 2nd say it, and
> finally give it an accurate title."

All of our winners had something to say.

Handler, a pathologist, said this:

> "If a physician must do something—or the patient feels he must do something—consider a mustard plaster. The patient will know something is being done. It will keep him busy while nature effects a cure."

Humor has its place, and Handler has used it well to say what we sometimes need to be reminded of.

Another man in another time, this one a clinician, said it this way:

> "It is a great mistake to suppose that Nature always stands in need of the assistance of Art . . . nor do I think it below me to acknowledge that, when no manifest indication pointed out to me what was to be done, I have consulted the safety of my patient and my own reputation effectually by doing nothing at all."—Thomas Sydenham (1624-1689).

This is what the men from Hennepin County had to say:

"(1) Splenic injury is common following abdominal trauma.

(2) Injury to the spleen must always be sus-

pected if the patient shows signs of shock or abdominal injury, especially if there are fractured ribs on the left or other signs of injury to the left side of the trunk.

(3) Splenic injury may be insidious or delayed in its manifestations and, in lieu of exploration, expectant observation should be carried out for at least seven days in any case of moderate to severe trauma to the left side of the trunk.

(4) As an isolated injury, a traumatically ruptured spleen does not result in a great blood requirement or in great morbidity or mortality. These sequelae are usually the result of other associated injuries sustained at the time of the accident.

(5) Pedestrian injuries carry a higher morbidity, mortality, blood requirement and longer hospital stay than other types of injury.

(6) Anticoagulation is not indicated except for specific complications following splenectomy for traumatic rupture.

(7) The entity of spontaneous rupture of the normal spleen is nonexistent and probably represents overlooked trauma."

And this is part of Doctor Milroy's message:

"In the late winter of 1858 near Redwood Falls, Minnesota Territory a dying Indian mother gave birth to her fifth child, a boy, who later, as a man, would distinguish himself as physician, author, lecturer and leader of his people. However, until the boy could earn a more dignified name he had to bear the name "Hakadah," meaning "the pitiful last."

"About four years later this lad was given a name to be proud of: one that foretold his future success and was determined by a lacrosse contest. To the camp of Mankato or Blue Earth on the Minnesota River, several bands of the eastern Dakotas had come for midsummer contests and festivities. This season the most important event was the lacrosse game between the Kaposia and the Wahpeton bands. With about fifty players on each side, what a contest this must have been! After a long struggle the Wahpetons were victorious when one of their players carried the ball across the opponents' goal line. To the victors went the privilege of giving a new name to one of their worthy little warriors. At a ceremony following the game the little boy, Hakadah, was brought to the center of the circle and received the name Ohiyesa: winner, or one who advances."

Saying It

I have given these excerpts of the winners' prose because the excerpts illustrate that there are different ways of saying things, each effective in the right setting. None of the authors, incidentally, used the traditional IMRAD (Introduction, Methods, Results, and Discussion) approach. And neither do you if you submit an article to this journal. We ask only that you present your message, or argument, or evidence logically and clearly. Whether your combination of words will explode in our minds remains to be seen.

Richard L. Reece, M.D.
Minneapolis, Minnesota

Idiopathic Scoliosis*

THE LOSS OF functional spine stability and adverse cosmetic effects resulting from idiopathic scoliosis are often associated with impairment of pulmonary and cardiac function and emphasize the need for early diagnosis and treatment. Basic and clinical scoliosis research has yielded valuable information concerning genetic influences, structural alterations, and the efficiency of treatment methods to correct the spinal deformity. For those of us not actively involved with scoliosis treatment requiring specialized training and continuous exposure, a basic understanding of its clinical course and early detection is essential to insure prompt and adequate treatment of patients and their families.

Certainly Minnesota is fortunate to have such medical pioneers in the care of crippled children, as Arthur Gillette and Carl Chatterton, when the active treatment of scoliosis was in its infancy. Their early leadership and the development of the Gillette Children's Hospital for Crippled Children created one of the nation's leading centers for the study and treatment of scoliosis. Under the guidance of Doctors John Moe and Robert Winter an active scoliosis service at Gillette Children's Hospital has been developed and maintained to care for affected patients and increase our knowledge about this condition.

With a continued multidisciplinary approach to the problems of scoliosis we shall hopefully advance from a successfully treatable disorder to a preventable one.

Lee C. Detenbeck, M.D.
Rochester, Minnesota

*See page 529.

The Specialized Orthopedic Surgery Program at Gillette Children's Hospital

When Gillette Children's Hospital moved to its present location in Phalen Park in St. Paul, its first concern was as it still is, the proper care of the child handicapped or crippled by an orthopedically improvable condition. The orthopedic staff was concerned with this child's welfare and there was no movement nor attempt to segregate any special orthopedic deformity or disease to any specific staff member.

In 1947 after a meeting of a newly formed small orthopedic group (The Contemporary Orthopedic Club), a Gillette staff member of the Club became interested in the problem of scoliosis. To him it became quite obvious that scoliosis was not as well treated nor managed at Gillette Children's Hospital as it was at the Hospital for Ruptured and Crippled under Dr. John Cobb nor as it was treated at the Milwaukee Children's Hospital under the care of Dr. Walter Blount and Dr. Al Schmidt.

On his return from this meeting he asked the Chief of Staff, Dr. Carl C. Chatterton, if it was possible to establish a scoliosis service at Gillette. The positive answer was quickly forthcoming.

There were some restrictions requested by Dr. Chatterton. The child should not be subjected to extensive surgical procedures which would endanger his survival. Fortunately, this was the era of rapid transition to good surgical care, to better anesthesia, blood replacement, and improved knowledge of surgical physiology, most of which were the aftermath of World War II.

It was an easy step in the surgical treatment of scoliosis to obtain supervision of anesthesia from the anesthesiology department of the University of Minnesota. The newly formed blood bank of the Red Cross Unit of St. Paul provided an ample supply of well matched blood. The danger of operative mortality from extensive surgical procedures on the spine became markedly decreased.

The scoliosis service at Gillette Children's Hospital thus became a reality, under the supervision of Dr. John Moe in January of 1948. Within three months there were 25 scoliosis patients in the hospital, all candidates for surgical correction.

Because of lack of experience, much advice was asked of the current scoliosis authority, Dr. John Cobb of the Hospital for Ruptured and Crippled in New York City. Dr. Cobb was magnanimous in his effort to help.

Since those early days of a subspecialty service in orthopedic surgery at Gillette Children's Hospital, many changes have occurred. The scoliosis service has enlarged and has become one of the nation's centers. Other subspecialty services have been established including club feet, hand problems, amputees, hip disabilities in children, cerebral palsy and myelomeningocele. The last two have become increasingly important for they have been neglected in the past, much as scoliosis had been neglected.

Early diagnosis is the key to quality treatment. The obstetrician must learn to evaluate the newborn infants hips. If there is a question as to hip dyplasia or subluxation, the orthopedic surgeon must be consulted. The pediatrician must be likewise knowledgeable. Myelodysplasia must be recognized at birth and a knowledgeable neurosurgeon and orthopedic surgeon must see the infant within a few hours of his birth.

With this type of progressive approach, pediatric orthopedists have now learned to control or cure conditions considered hopeless 25 years ago.

The Staff of Gillette Children's Hospital
St. Paul, Minnesota

Meeting

Southern Minnesota Medical Association Annual Meeting, September 23, 1972, in Austin, Minnesota.

New Methods of Pain Relief

Intractable pain remains one of the most serious of our unsolved medical problems. Recent advances in the therapy of pain have been in two areas: The first is the development of stereotactic percutaneous cordotomy. This procedure can be done with the patient awake and even seriously debilitated patients can be treated. The procedure is performed under fluoroscopic control and a needle is inserted through the C2 neural foramen laterally into the subarachnoid space. The spinal cord is visualized by the use of emulsified pantopaque and the needle directed into the anterior lateral quadrant of the spinal cord. The spinothalamic tract is then destroyed by electrocoagulation. The overall success rate and complication rate is approximately the same as for open surgical cordotomy, but the procedure is much simpler for the patient and a major operative procedure is avoided by this technique.

The newest investigative area in pain control is in the use of various forms of electrical stimulation for the relief of pain. The electrical stimulation can be used in several ways. External stimulation simply applied on the skin, over motor points, peripheral nerves, or bony prominences will relieve many kinds of pain on a temporary basis. Most patients find the devices too cumbersome for general use, but they are quite effective in temporary pain relief. A second form which has proved very successful, is peripheral nerve stimulation. Permanently implanted electrodes attached to a small radio receiver are placed around the injured nerve from which the pain is emanating. By external controls the patient is able to stimulate transcutaneously and produce sensation in the distribution of the affected nerve which successfully blocks pain. Slight hypesthesia is usually produced, but no disability of motor function. Pain relief after stimulation may be prolonged up to several hours so that the use of the device is intermittent.

Another area where permanent implantation of a stimulating device is employed is in stimulation of the posterior columns. Again a small electrode is placed over the posterior column and attached to a subcutaneously implanted radio receiver. Transcutaneous stimulation from an external power source then produces a tingling sensation in the body below the level of the implantation. This sensation has been successful in blocking pain of a variety of causes: chronic low back syndrome secondary to arachnoiditis, spinal cord injury, phantom limb, cancer and rheumatoid arthritis.

While these procedures are still in the investigative stage, the results obtained so far are highly encouraging. The stimulation procedures seem to be much more effective in normal individuals without significant psychological overlay and the majority of the failures of stimulation have come in patients with serious psychiatric problems. The presence of drug addiction is not a contraindication, but is a problem which must be solved separately after the pain relief is affected.

The next area for exploration in stimulation for pain control is in the use of permanently implanted electrodes within the brain. A great deal of experimental work has been done in animals which indicates that there are several areas in which chronic brain stimulation may be useful for the relief of pain and possibly chronic affective disorders. This work is still very much in the investigative stage, and only a few patients have been so treated. However, preliminary results are highly encouraging and it is expected that this field will develop as the instrumentation is improved.

Don M. Long, M.D.
Minneapolis, Minnesota

Do not do unto others as you would that they should do unto you. Their tastes may not be the same.—George Bernard Shaw

Review—

Sigmoidal Complications of Left Ovarian Enlargement

RAYMOND A. LEE, M.D.;* LOUIS F. SILVERMAN, M.D.† and JOSEPH H. PRATT, M.D.*

DIAGNOSIS, THERAPY, and prognosis of ovarian tumors are predicated on etiologic and histologic factors. Because the ovaries are bilaterally symmetric organs, little thought usually is given to the significance of the side of involvement, other than where to place the abdominal incision.

Enlargement of the right ovary represents no appreciable mechanical hazard to the adjacent ascending colon, and the passage of solid or semiliquid stool rarely is embarrassed. The left ovary, however, is so situated that sigmoid colon and mesentery are in jeopardy should significant ovarian enlargement occur. This is especially true if the patient has had previous pelvic surgery and the bowel is adherent to the left adnexa. Impaired vascular integrity, bowel angulation, or interference with the passage of formed stool may result from the mechanical effects of left ovarian enlargement. Bowel adhesions or mesenteric invasion by the ovarian neoplasm increases the technical problems and associated risk of oophorectomy, and may even result in the necessity for sigmoidal resection.

We have recently had two cases in which an enlarged left ovary impinged on the sigmoid colon, adding appreciably to the technical problems of left oophorectomy and hence prompting this review.

Report of Cases

Case 1

A 28-year-old housewife with known thrombopathy presented with a three to four months' history of melena associated with nausea and an aching left lower quadrant abdominal pain. Ten days before examination she had experienced an acute exacerbation with nausea, emesis, dysuria, and a temperature of 101 F. Her past medical history was relevant in that a total abdominal hysterectomy and right salpingo-oophorectomy were performed five years previously. The postoperative course was complicated by hemorrhage requiring reexploration and ligation of the right uterine and both hypogastric arteries to achieve hemostasis. She subsequently underwent uneventful repair of a vesicovaginal fistula here.

She had a long, cylindrical mass in the left lower quadrant of her abdomen. On pelvic examination the mass was demonstrated to be about 12 cm in diameter, cystic, soft, and semimovable. Routine laboratory examination was unremarkable. Proctologic examination to 15 cm above the dentate line demonstrated the presence of a smooth, soft, probably cystic extrarectal mass. Cystoscopic examination revealed an extrinsic deformity of the left side of the bladder, and excretory urography confirmed the presence of a left lower abdominal soft-tissue mass.

Laparotomy revealed the pelvis mass to be a hemorrhagic cyst of the left ovary, 15 by 10 cm in size. The sigmoid was adherent over the top and lateral to the cyst so that the cyst extended into the mesentery of the sigmoid. With considerable difficulty, sigmoid and mesenteric vessels were mobilized from the dome of the cyst, resulting in two rents of considerable size in the mesentery but not grossly impairing the blood supply to the colon. The cyst was removed intact and proved to be a hemorrhagic endometrioma. The postoperative course was uneventful, except for nausea lasting four days, and the patient was dismissed from the hospital on the eighth postoperative day.

Case 2

A 40-year-old obese housewife, gravida 2, para 2, presented with a six months' history of urinary incontinence and recent onset of rectal pain and blood-tinged rectal discharge. Three years prior to admission she had undergone dilatation and curettage followed by total abdominal hysterectomy and right salpingo-oophorectomy. The pathologic diagnosis was reported as proliferative endometrium and chronic cervicitis. The right tube and ovary were not remarkable.

A lower abdominal mass was palpable, and pelvic examination revealed it to be an eight by 10-cm semimovable left pelvic tumor. Barium enema demonstrated the sigmoid colon to be pushed to the right by an extrinsic soft-tissue mass.

At laparotomy, a 15 by 10-cm multilocular benign serous cystadenoma of the left ovary was found; it was pushing the sigmoid colon far to the right. Careful, tedious mobilization was required to allow intact removal of the cyst. There was no damage to the adherent colon, and its vascular supply seemed adequate. The postoperative course was uneventful.

Material

Three hundred forty-nine cases of left oophorec-

Read at the meeting of District VI of the American College of Obstetricians and Gynecologists with the Minnesota Obstetrical and Gynecological Society, St. Paul, Minnesota, November 14, 1970.

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tomy with additional procedures involving sigmoid colon or sigmoid mesentery were reviewed for the 10-year period, 1956 through 1965. In this group were 40 cases where the integrity of the sigmoid was sufficiently jeopardized for the surgeon to note the need either for careful mobilization or for more extensive procedures involving the sigmoid (Table 1).

TABLE 1
Presenting Symptoms of Complications From Left Ovarian Enlargement

Symptoms	Malig.	Benign	Inflam.	Total
Gastrointestinal				
Altered bowel habits	5	4	2	11
Bloating	4	2	1	7
Melena	2	2	1	5
Cramping	2	0	2	4
Nausea	2	1	1	4
Weight loss	2	1	0	3
Gynecologic				
Abnormal bleeding	1	2	3	6
Dyspareunia	0	2	1	3
Dysmenorrhea	0	1	0	1
Miscellaneous				
Abdominal pain	4	5	7	16
Fever	1	0	3	4
Hematuria	1	1	0	2

Age at the time of operation ranged from 14 to 85 years, with an average of 47 years. Six patients were 35 years old or younger. Fifteen of the patients had malignant lesions, of which four were bilateral. Seventeen cases involved unilateral benign tumors, while eight were inflammatory masses, of which two were bilateral.

The presenting symptoms were varied and are described in Table 1. The patients frequently had more than one primary complaint. Abdominal pain could be expected to be a major complaint of a group of patients with ovarian tumor, and it was the most commonly elicited symptom. It was generally in the lower abdomen and frequently in the left lower quadrant.

The most interesting finding in this group of patients is the high incidence of bowel symptoms. Eleven of the 40 patients had noted a change in bowel habits, either constipation or thin stools, or even diarrhea, but almost 50% of those with benign lesions had symptoms, presumably because their cystic masses were larger and caused greater mechanical problems. There were 23 additional complaints of bloating, nausea, and melena, all presumably due to the ovarian enlargement encroaching upon the mesentery of the sigmoid or compromising the lumen of the bowel. This is a distinct contrast to the paucity of the gynecologic complaints (10 of 40), six of which were abnormal bleeding. Approximately half the patients knew a mass was present.

Physical findings usually involved the presence of a mass, which was palpable abdominally in 26 cases and by pelvic examination in 40. There were no enormous cysts in this group; the average diameter was 10 to 12 cm and, generally, these pelvic masses were "soft" or "cystic" in nature.

Routine laboratory studies were of little diagnostic aid. Inflammatory conditions were characterized by elevated leukocyte counts and sedimentation rates. Hemoglobin values ranged from 10.1 to 14.5 gm. Leukocyte counts varied from 2,600 to 14,600 (interestingly, the low value was in a patient with an acute tubo-ovarian abscess). Routine urinary examination followed the anticipated pattern, with both malignancy and inflammatory disease producing significant proteinuria and hematuria, but few changes were associated with the benign lesions. The average sedimentation rate in malignancy was 42.4 mm in one hour, ranging from 13 to 110 mm. In those patients with inflammatory disease, sedimentation rate averaged 36.7 mm, varying from 13 to 90 mm, while sedimentation rate in benign ovarian neoplasia averaged 15.6 mm, ranging from 3 to 30 mm.

The results of proctoscopic examination, colon Xray, and urologic examinations are detailed in Table 2. Hysterosalpingography was performed in one patient who had an acute tubo-ovarian abscess and defined obstruction to the left tube.

TABLE 2
Results of Preoperative Diagnostic Procedures

Proctoscopic examination		16
Helpful	11	
False-negative	4	
Equivocal	1	
Colon x-ray		11
Helpful	8	
False-negative	2	
Equivocal	1	
Urologic examination		15
Helpful	9	
False-negative	5	
Equivocal	1	

Technical problems encountered at surgery are described in Table 3. In general, it is necessary to use sharp dissection to mobilize the sigmoid with its mesentery from the underlying left adnexal mass. Identification of the left ureter is also necessary before resection is possible. The sigmoid

and its mesentery may require repair secondary to the surgical trauma. Because of impairment of the blood supply or direct invasion of the sigmoid by the ovarian enlargement, primary sigmoid resection may be necessary. This was necessary in eight instances.

TABLE 3
Technical Problems Encountered at Operation

Problem	No.
Difficulty mobilizing sigmoid	23
Sigmoidal trauma to mesentery	22
Sigmoid resection	8
Bowel repair	9

Discussion

A significant difference in operative risk prevails when comparing oophorectomy with sigmoid resection. As an indication of that difference, hospital mortality figures for these procedures were compared over this same 10-year span. Oophorectomy was associated with a hospital mortality rate of 0.65%, while that for sigmoid resection was 2.76%.

It is apparent that the gynecologic surgeon must be prepared to recognize and treat intestinal disease or that he must have available consultation by a gastrointestinal surgeon.

In the past, many surgeons thought that they could not operate on the unprepared colon without high morbidity and mortality. Herrington and his co-workers[1], and Schnur et al.,[2] have shown that this is not true. Herter and Slanetz[3] reviewed the histories of 1,042 patients who had undergone resection of the colon, some of whom had received antibiotic preparation and some only cleansing enemas. They concluded that, if the anastomosis was made in the peritoneal cavity, postoperative complications occurred at the same ratio in both groups. Therefore, if one finds himself faced with the need to perform a resection of unprepared colon, he should proceed with this treatment unless the intestine is full of hard stool.

In the course of hysterectomy in the premenopausal female, preservation of some ovarian tissue is a common goal. In the absence of ovarian pathology necessitating sacrifice of the right ovary, it appears reasonable to propose that selective removal of the left ovary may forestall the later development of sigmoid complications should ovarian enlargement subsequently occur.

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Catatonic Syndrome

The objective changes associated with this syndrome include negativistic reactions, automatic changes, mutism, flexibilitas cerea, and episodes of pathognomonic excitement. Although the catatonic syndrome is seen most frequently in certain psychologic disturbances, such as schizophrenia, it has also been associated with numerous other central nervous system disturbances. Aside from the associated psychogenic relationships, typical catatonic syndromes may occur as a result of trauma to brain tissues. Such psychogenic states have occurred with subdural hematoma, in multiple, discrete, and coalescent areas of the encephalomalacia, and in multiple petechial hemorrhages. Catatonic states have also occurred in acute demyelinization of the central nervous system, in serous meningitis, or in other conditions with which there was an associated increased intracranial pressure.

According to Micheels, several workers have been able to produce a catatonic syndrome in experimental animals, using bulbocapnine, carbon dioxide, nitrogen, and other chemical or biochemical substances. On the basis of these experiments, certain writers have suggested that catatonia is a general reaction occurring as a result of alteration of metabolic functions.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

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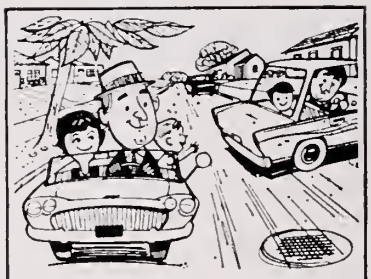
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Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

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Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

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1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomyc hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water But when 4 grams or more per day is given, Lincocin should be diluted in n less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

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nsitive to penicillin or cephalosporins,
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tigenicity with these compounds.
owever, hypersensitivity reactions
ve been reported, some of these in
tients known to be sensitive to
nicillin.

ell tolerated at infusion site: Lincocin
travenous infusions have not
oduced local irritation or phlebitis,
ien given as recommended. Lincocin
usually well tolerated in patients who
e hypersensitive to other drugs.
evertheless, Lincocin should be used
utiously in patients with asthma or
gnificant allergies.

patients with impaired renal function,
e recommended dose of Lincocin
ould be reduced to 25—30% of
e dose for patients with normal
dney function. Its safety in
egnant patients and in infants
ss than one month of age has
t been established.

ncocin may be used with other
timicrobial agents: Since Lincocin
stable over a wide pH range, it is
itable for incorporation in
travenous infusions; it also may be
administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatr it. *Skin and mucous membranes*—Skin ra s, urticaria, vaginitis, and rare instances o v exfoliative and vesiculobullous dermatitis ve been reported. *Liver*—Although no dire e lationship to liver dysfunction is establi d, jaundice and abnormal liver function as (particularly serum transaminase) have en observed in a few instances. *Cardiovas ar*—Instances of hypotension following p n teral administration have been repo d, particularly after too rapid IV admin a tion. Rare instances of cardiopulmonar ar rest have been reported after too rapi V administration. If 4.0 grams or more ad n istered IV, dilute in 500 ml of fluid ad administer no faster than 100 ml per l ur *Special senses*—Tinnitus and vertigo ve been reported occasionally. *Local reac ns*—Excellent local tolerance demonstrat to intramuscularly administered Linc in (lincomycin hydrochloride). Reports of in following injection have been infreq ly Intravenous administration of Lincoc in 250 to 500 ml of 5% glucose in dis ed water or normal saline has produce no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500* Capsules—bottles of 24 and 100. *S le Solution, 300 mg per ml*—2 and 10 ml als and 2 ml syringe. *Syrup, 250 mg per* —60 ml and pint bottles.

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Dr. Carl C. Chatterton and Gillette Children's Hospital

J. H. MOE, M.D. and R. B. WINTER, M.D.

THE ORTHOPEDIC SURGEON of today enters his practice after four or more years of concentrated study, instruction and practice of his specialty. He must demonstrate his capabilities in this specialty by passing a rigid examination before he is certified as a specialist.

In the early years of this century, the training of the orthopedic surgeon was quite different. Once he decided on an orthopedic career, he sought areas and institutions where he could be exposed to men whose primary interest lay in this field. He endeavored to obtain an association with such men and to act as their assistant. Often, he hoped to become a partner to such a man.

Such were the aims and ambitions of Dr. Carl Chatterton when he first came to St. Paul, Minnesota in 1910 to assist in the care of indigent crippled children at the Minnesota State Hospital and during the following year when he was an intern at the City and County Hospital. He had a good friend in Dr. Ancker during that year of internship and he took Dr. Ancker's sage advice that, "If you watch your P's and Q's you might land a job with Dr. Gillette."

Dr. Arthur Gillette

Dr. Arthur Gillette was a pioneer orthopedic surgeon. He attended Hamline University in St. Paul and later the Minnesota Hospital College from 1883 until 1885. He transferred his allegiance to the reorganized St. Paul Medical College in 1886, the year he was graduated. He specialized in the orthopedic care of the crippled and deformed child and his intense interest was in the field of children's orthopedics. He initiated the thought of a state controlled and financed institution for the care of the indigent crippled child in 1897 when he appeared before the legislative body known as the Minnesota Conference of Charities and Corrections. He read to them a paper entitled "The Duty of the State to its Crippled and Deformed Children."

Dr. Gillette was helped in his endeavors by a crippled girl named Jessie Haskins who the year before had presented a plea to that same legislative body for state help to the indigent crippled



Fig. 1—Gillette Children's Hospital in the horse and buggy days, approximately 1910.

child. The paper in 1897 read by Gillette was followed the same year by another plea by Jessie Haskins begging them for help.

The joint efforts of this crippled girl and Gillette met with success, particularly when he offered his services free to give orthopedic help to the crippled child. A bill was passed by the legislature of Minnesota providing such a state aid—the first state in the Union to do so.

The state law to provide for the care, education, and treatment of the indigent, crippled and deformed children of the State of Minnesota was passed in 1897. The Board of Regents of the University of Minnesota was given the power to act in its formation and supervision and $5,000 was appropriated for its support.

The City and County Hospital in St. Paul was its first home. A ward was given exclusively for the care of these children at a rate so low that is was possible to care for 80 children during the first two years of the institution's existence. Appropriations then came more easily and the work increased so rapidly that the ward became filled. The necessity of a separate building became apparent. A structure adjoining the City and County Hospital was then used. This structure was donated to the State of Minnesota by the City of St. Paul in 1907. A group of St. Paul citizens, the Commercial Club and the Business League, responded the same year with a purchase of twenty-three acres of land near the outskirts of St. Paul. This was also given to the State. This land was adjacent to what later became Phalen Park and is the present site of Gillette Children's Hospital.

In 1907 the State Board of Control was put in charge of the Minnesota State Hospital for Indigent Crippled and Deformed Children. In 1909, $55,000 was appropriated to construct the first portion of the present building on the land adjoining Phalen Park. In 1913, $60,000 more was appropriated to build an addition. The same year the property adjoining the City and County Hospital was given back to the City of St. Paul and all the children were transferred to the new building near Phalen Park.

Dr. Carl Chatterton

Dr. Carl Chatterton was born in the small country town of Peterson, Iowa in 1885. His father, Allen Smith Chatterton, (Mother—Jennie) was a general practitioner, a country doctor of the type now almost extinct.

He took his medical education at Northwestern University and during his senior year he saw a message on the blackboard indicating that the City and County Hospital in St. Paul offered an examination for interns. Dr. Chatterton and three of his classmates took this examination and shortly thereafter, Dr. Ancker came to Chicago to tell them of the fine internship at his hospital. Two years were offered, one in orthopedics at the Minnesota State Hospital, the other at the City and County Hospital. Dr. Chatterton was interested in the thought of helping the crippled children and he accepted these offers although prior to this he had planned on obstetrics.

During these years he gained the confidence and friendship of Dr. Gillette. At the completion of his internship he was offered an association with this well known orthopedic surgeon. This he proudly accepted.

He retained this association until the death of Dr. Gillette on March 24, 1921. He developed a sound and lasting knowledge of general orthopedics but his love for children's orthopedics predominated.

With the death of Dr. Gillette came the ap-



Fig. 2—Dr. Chatterton and a patient with tuberculosis of the spine, approximately 1930.

pointment of Dr. Chatterton to the position of Chief of Staff of the Minnesota State Hospital for Indigent Crippled and Deformed Children.

It was renamed in 1925 by an act of the legislature to honor Dr. Gillette in recognition of his work on behalf of the crippled child. Since then, it has been known as Gillette Children's Hospital. Dr. Chatterton served as its Chief of Staff from 1921 to 1955.

More appropriations for further additions were authorized. In 1925, the Michael Dowling Memorial Hall was donated by Dowling and the Bankers Association of St. Paul. This added an auditorium with an adjoining library, school, and classroom facilities.

Chatterton continued as Chief of Staff until 1955 when at the age of 70 he made the decision to resign as Chief. He has continued to be on the active Orthopedic Service Staff and his interest and attention to the orthopedically handicapped child remains undimmed. Since his semi-retirement the growth and expansion of Gillette Children's Hospital continued.

For many years following World War I the administration of the hospital was in the capable hands of Miss Elizabeth McGregor while the school of Nursing was supervised by her sister, Miss Margaret McGregor. It was during these years that many of the happy memories of Gillette Children's Hospital developed. Dr. Chatterton still vividly recalls the performing parrot, Polly, who could imitate the children and whose talking abilities caused much laughter and often some concern.

Dr. Chatterton recalls also the days of the influenza epidemic in 1919 when many children died in the hospital; some days as many as four or five. Children who had skeletal and joint tuberculosis were easy victims of this devastating epidemic.

While under the direction of Miss McGregor. the out-patient department was relocated and recreation room facilities were added. In 1949, when Miss Elizabeth McGregor retired, Miss Jean Conklin became administrator of Gillette Children's Hospital. Under her direction the hospital program has continued to grow. In 1959, a new Service Wing was constructed which included an x-ray laboratory, dentistry, speech, and hearing facilities, photography laboratory, central supply, and a new braceshop. In 1960 a surgical wing was



Fig. 3—Dr. Chatterton making rounds, April, 1970.



Fig. 4—Dr. Chatterton standing beside the painting of Dr. A. J. Gillette, founder of the Hospital.

built which included two new operating rooms, remodeling of one old operations room, a new cast room, a new postoperative recovery room, a doctor's lounge and locker room, and offices.

Gillette Children's Hospital

In 1959, the legislature passed a law enabling Gillette Children's Hospital to collect on hospital insurance carried by the parents of the patients if such insurance was available. In 1967, the legislature passed a law enabling Gillette Children's Hospital to bill parents according to their ability to pay and to collect from all other available sources including insurance companies and federally-financed health programs. In 1967, the legislature also passed a law creating the Medical Education and Research Account Fund allowing surgical fees to be collected by the doctors for this fund to be used in medical education and research.

Many orthopedic surgeons have received their training in children's orthopedics at Gillette Children's Hospital under Dr. Chatterton since residents first came under his supervision there in 1921. Many also have spent a period of their internship there and some of them thereby developed an interest which led them to continue training in orthopedic surgery. The present orthopedic staff is largely made up of men who have spent a year of their training in children's orthopedics at this institution.

Throughout the many years that Dr. Chatterton was Chief of Staff at Gillette Children's Hospital, he was first and foremost a superb teacher. He is Emeritus Associate Professor in Orthopedic Surgery at the University of Minnesota. He is a senior member of the American Orthopedic Association. He was a founding member of the Central States Orthopedic Society, later renamed the Clinical Orthopedic Society. He also founded the Minnesota-Dakota Orthopedic Society.

After sixty years of continuous service to the Crippled Children of the State of Minnesota, Dr. Chatterton is now retiring from active participation in the care of Gillette Children's Hospital patients.

His interest in their future remains unaltered. We hope that Minnesota will always be a place where such pioneers can see their dreams fulfilled.

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The Development of an Alcoholism Unit in a Private General Hospital

THE REVEREND PHILIP L. HANSEN*

IF A PERSON IS sick enough to die from the uncontrolled use of alcohol or to destroy his life and those he loves, it would seem that he ought to be considered sick enough to be admitted to a community hospital and to receive the kind of care he deserves.

In 1944, a special committee of the American Hospital Association recommended that "The primary point of attack (on alcoholism) should be through the general hospital. Because of the completeness of its facilities and of its accessibility, it is the logical place to which an alcoholic or his family would turn." This statement was approved by the American Hospital Association in 1957. It has only been recently that this concept has been put into practice. St. Mary's alcoholism unit in Minneapolis opened in December 1968, and the unit at Northwestern began to receive patients on July 27, 1970. Both of these units were filled in a week and have remained full. I am working closely with St. John's Hospital in St. Paul and St. Cloud Hospital in St. Cloud both of which soon will start programs similar to ours.

The unit at Northwestern Hospital would not exist were it not for the fact that a few staff physicians and others realized that alcoholism is treatable. In a number of instances they had had experience, within their family, of successful treatment elsewhere, so they became the driving force in supporting Northwestern's treatment unit.

Current Staffing

The most difficult aspect of beginning such a unit is the staffing. At present I have the following personnel, most of them arrested alcoholics: a head nurse, a psychologist, three counselors on alcoholism, a person as liaison between Alcoholics Anonymous and outpatient resources, and a graduate theologian working in the outpatient follow-up program. Besides this first line staff there are the other nurses, L.P.N.'s, clergy, orderlies, and so on. I hire the people who will work in our unit because I want people who have some empathy for the alcoholic and his illness. To be effective in this work you must unlearn your discipline and be willing to learn some new skills. A good therapist may be found among the trades or even among the clergy. Northwestern Hospital had never hired a clergyman, and when the word came that a preacher was going to head up the alcoholism treatment unit there was some vigorous criticism. Nevertheless, this is not the kind of work for which you can hire people on the basis of a standard job application. You must have some measure of their ability to communicate with people, and they must have some insight into the dynamics of this illness, alcoholism.

Program

The first objective in treating the alcoholic is to receive the patient and keep

*Director, Alcoholism Unit, Northwestern Hospital, Minneapolis.

him alive. At this point everyone works to support the physicians and nurses. Detoxification is the first step, and perhaps the easiest part of the entire treatment routine. The basic goal is to withdraw the patient from all mood-modifying chemicals as safely and quickly as possible. This is the task of the medical staff and they do it effectively. Almost all of the detoxification is done in the same hospital room the patient will occupy in the weeks to come. In 120 admissions up to the end of October at Northwestern Hospital only three patients were moved to intensive care or to another medical unit because of complications. Nevertheless, the risk of complications is one of the things that has convinced me that alcoholism should be treated in the community hospital. The availability of the broad range of medical services is very reassuring to everyone on the unit's staff. When the patient arrives, the vital statistics have been gathered, and the doctor has been consulted, the nurses move into one of the routines that has been established, and the early part of treatment is begun.

When the patient has been detoxified he enters the flow of the treatment program. At 9 a.m. each weekday one of the 12 steps of Alcoholics Anonymous (AA) is lectured on and discussed. Then general group therapy sessions begin. After lunch there is a lecture or audiovisual presentation. The latter part of the afternoon is spent reading, going for a walk in the park, or visiting with the counselor. Each evening there is either a lecture by some consultant or an activity of AA that involves the outside community. Some of the finest communicators in the field of alcoholism come in and talk to the patients. Early in the patient's hospital stay, we inform AA (in the area where the person lives) and tell them that the patient is in the treatment unit. An AA representative is asked to contact the patient and his spouse, who will be introduced to AA in their home area while treatment continues at Northwestern.

Two afternoons a week the spouse is asked to come to the hospital for the couple's group therapy. This procedure has proven to be very helpful. On Sunday the patients who choose to do so are taken to church near the hospital.

No patient is admitted to the unit unless they agree to stay for a minimum of 21 consecutive days. This does not mean it is a 21-day treatment, but rather a minimum open-end stay. The average stay is about one month, with the women remaining a bit longer than the men.

If the patient's hospitalization program does not cover treatment for alcoholism, the Hospital requires a cash deposit to cover a minimum stay of 21 days. This causes us some frustration when the patient wants in, but also prevents many financial problems after the patient has left. We have had excellent support from the hospitalization insurance companies, which only further supports the premise that this illness should be treated in the hospital. Every patient in our unit is admitted with a diagnosis of alcoholism, which is exciting in itself when we recollect how long the physician has had to go through diagnostic and moral gymnastics to get the patient into the hospital for detoxification. Each bed in the alcoholism unit is an acute bed and the cost is the same per day as any other acute bed in the hospital.

The Unit's task is to take a chemically dependent person, get him well physically, and then prepare him to go back to society to live and to cope as comfortably as possible with reality. We try to use every available resource and skill to do this. The greatest healing is done by the patients themselves. What we on the staff attempt to do is create a healing milieu.

Physical Setting

We inherited a brand new circular unit not unlike any circular unit of us

has seen. We took the nurses' station out of the middle and put it near the entrance. In the center is a lounge area. When the alcoholic patient goes to treatment, part of his problem is dehumanization and desocialization. The patients in the unit are together whether they like it or not, and this aspect of treatment I would hate to give up. It is too easy for the patient who has been running away, to run away to his room at the end of some long hall. We have no private rooms, either, because they, too, permit desocialization to continue.

Cooperation with the Medical Staff

Cooperation from the medical staff has been excellent. Fifteen doctors from several specialities have volunteered to take patients who have no staff physician. Staff physicians are encouraged to follow their patients through the treatment program. At times the system may be cumbersome, but in the long run there will be many doctors well versed in detoxification and the dynamics of such treatment. Teamwork with lay counselors is essential. This is a good example of using paramedical personnel to the utmost.

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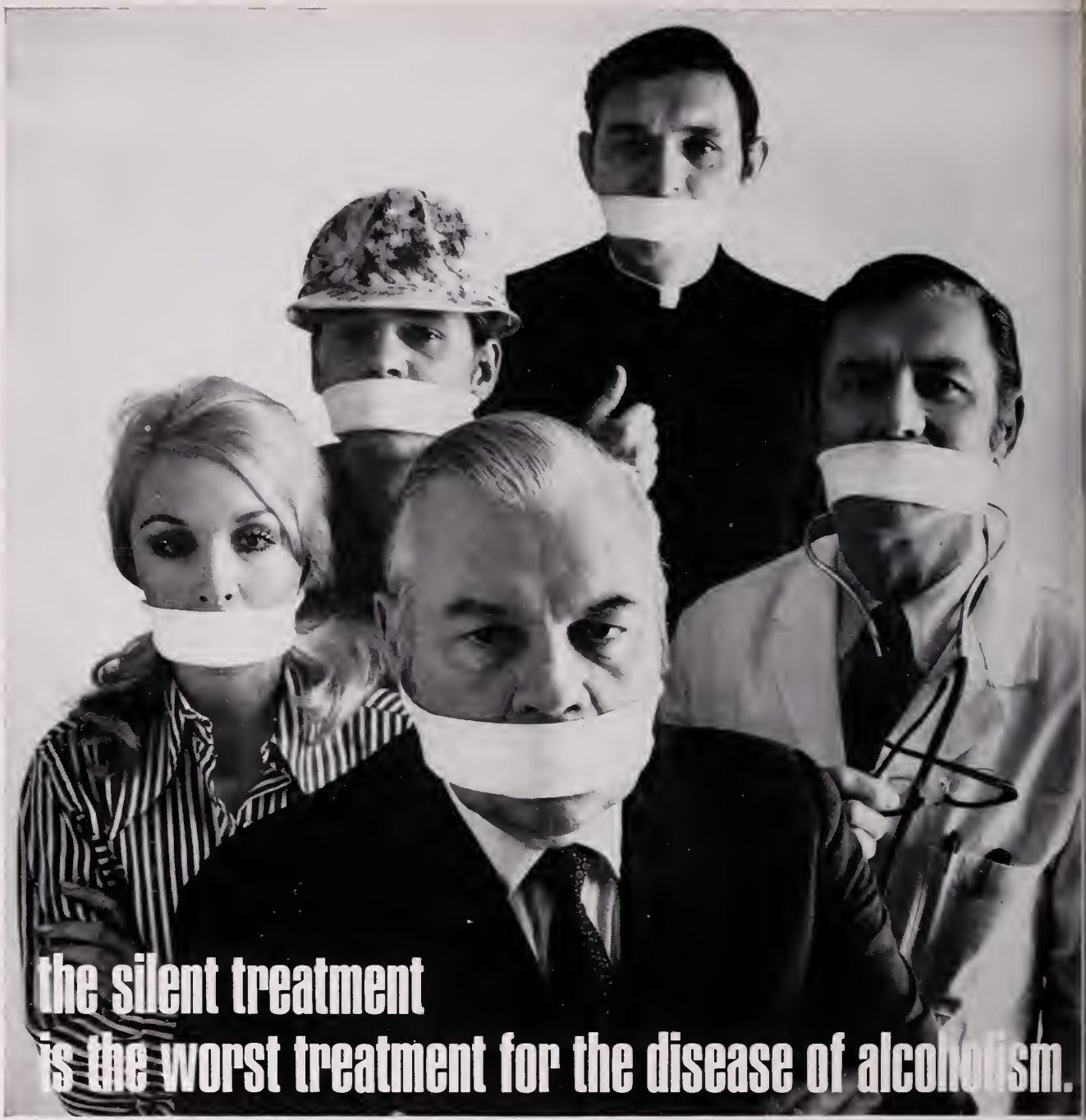
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When one out of 20 employees in America—including executives—has alcoholism, it's time for some plain talk about alcoholism. The alcoholic's family, friends and employer may mean well, but the silent treatment is no way to treat a disease. And alcoholism is a disease from which recovery is possible, rather than a moral weakness for which the alcoholic should be pitied—or fired. It's a disease which ranks with heart disease, cancer and severe mental disorders as a public health menace.

The National Council on Alcoholism has pioneered in setting up joint union-management alcoholism programs. In these programs, industry is achieving *recovery rates averaging 60 to 70 percent*. Management profits by retaining its experienced employees and regaining lost productivity—estimated at six billion dollars. Unions profit by increasing health and welfare protection for members and keeping them in the active work force.

If you think alcoholism is affecting your business, **talk it over with the Director of Labor Management Services, National Council on Alcoholism, 2 Park Avenue, New York, N.Y. 10016.**

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50 mg. Tablets

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brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used caution in patients about to undergo surgery of the biliary t

Patients Receiving Narcotics. Talwin is a mild narcotic antago Some patients previously receiving narcotics have experienced withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administ to patients prone to seizures; seizures have occurred in a few patients in association with the use of Talwin although no cause effect relationship has been established.

Adverse Reactions: Reactions reported after oral administr of Talwin include *gastrointestinal:* nausea, vomiting; infrequ constipation; and rarely abdominal distress, anorexia, diar *CNS effects:* dizziness, lightheadedness, sedation, euphoria, h ache; infrequently weakness, disturbed dreams, insomnia, syn visual blurring and focusing difficulty, hallucinations (see *A CNS Manifestations* under WARNINGS); and rarely tremor, tability, excitement, tinnitus. *Autonomic:* sweating; infrequ flushing; and rarely chills. *Allergic:* infrequently rash; and ra urticaria, edema of the face. *Cardiovascular:* infrequently dec in blood pressure, tachycardia. *Other:* rarely respiratory depres urinary retention.

Dosage and Administration: *Adults.* The usual initial adult do 1 tablet (50 mg.) every three or four hours. This may be incre to 2 tablets (100 mg.) when needed. Total daily dosage should exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in a tion to analgesia, aspirin can be administered concomitantly Talwin.

Children Under 12 Years of Age. Since clinical experience in l dren under 12 years of age is limited, administration of Talwi this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have rec Talwin orally for prolonged periods have not experienced w drawal symptoms even when administration was abruptly dis tinued (see WARNINGS). No tolerance to the analgesic effect been observed. Laboratory tests of blood and urine and of liver kidney function have revealed no significant abnormalities a prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin o dosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and c supportive measures should be employed as indicated. Assiste controlled ventilation should also be considered. Although n phine and levallorphan are *not* effective antidotes for respira depression due to overdosage or unusual sensitivity to Talwin, r enteral naloxone (Narcan®, available through Endo Laboratorie a specific and effective antagonist. If naloxone is not available, r enteral administration of the analeptic, methylphenidate (Rital may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet con Talwin (brand of pentazocine) as hydrochloride equivalent to 50 g base. Bottles of 100.

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Special Article

Systematized Nomenclature of Pathology

Conversion to the Computer Language of Medicine

ARTHUR H. WELLS, M.D.*

A DESCRIPTION OF the unique characteristics of the Systematized Nomenclature of Pathology[1] (SNOP) follows. A few highlights of the gestational period of SNOP with results of the Field Trial Edition and its Visual Aid are covered. The story would not be complete without reviewing the frustrating experiences with the World Health Organization (WHO) and the Council on International Organizations of Medical Sciences (CIOMS).

You will forgive a recording of some of the successes which have spurred the committee on to establish a master system to contain the whole of clinical medicine. For one thing all hospital records should be in one code and for another medical science should not be handicapped by failing to develop a computer language of all of medicine, an accomplishment long overdue.

Unique Identity

The SNOP published in 1965 by the College of American Pathologists is indeed a unique classification, coding system and nomenclature of medical diagnostic terms. One could create a usable coding system of medical terms by attaching numeric equivalents to a haphazard collection of names of diseases and agents. For this one need simply to arrange these terms with their codes in alphabetic order. The Current Medical Information and Terminology[2] (CMIT) of the American Medical Association (AMA) could be an example. The CMIT serves a much needed purpose as an official dictionary with French, German and Spanish cross reference but not a storage and retrieval vehicle, let alone a computer language of medicine. Classification and definition are the essence of knowledge. Classification alone delimits entities, defines knowledge, exposes ignorance, advances understanding, permits comparison, reveals interrelationships, promotes varied generalizations and indicates areas of needed investigation and research. CMIT plus a Systematized Nomenclature of Medicine (SNOMed) based on SNOP would be a profound contribution to medical science. Current Procedural Terminology[3] (CPT) of the AMA may well be accepted as the fifth therapeutic and procedural field of SNOP.

SNOP as a Classification System

The SNOP was developed as a detailed classification of all of its entities as they relate to each other. The unique separation of the medical diagnostic terms into their basic linguistic components of site, visible alteration, physiologic activity and etiologic entity was the result of independent advice of two distinguished biometrions, E. Cuyler Hammond of the American Cancer Society, Inc. and Harold Dorn of the National Institutes of Health (deceased).

These four fields named Topography (T), Morphology (M), Function (F), and Etiology (E), became the basis for a skeleton of a decimal and duodecimal classification. With four digits, 9,999 groupings and entities can be placed in each field, beyond this alphabet letters can be used for the last two digits. The first edition has 22,428 entries in the combined alphabetic indices. Room was left in all fields, sections and groups for expansion.

Topography

For practical reasons including frequency of disease in certain sites and number of anatomic structures, Topography was arranged into 140 two-digit sites and areas. Each of these was expanded into a four-digit code which together contain over 4,000 detailed anatomic entities in the first edition. The practical need of a two-digit code for 140 sites necessitated the use of a duodecimal division. In the mid-sixties the most efficient computer handling of this was by the use of the single punches + and −. We called them X and Y. They required only one pass

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through the card sorter whereas alphabetic codes per se required two passes.

Our topology terms were taken from the internationally accepted "Nomia Anatomica." The decimal systems of M, F and E permit any degree of utilization depending on the interests of the user. Thus pure morphologists could use only Topography and Morphology or a psychiatric diagnosis could be reduced to one general term in the psychiatric field of Function or one of ten subgroup titles.

"Unit of Information"

An analysis of the defects of the Standard Nomenclature of Diseases and Operations[4] (SNDO) led to an attempt at creating a "unit of information" system of medical coding so basic in a linguistic code. An etiologic agent or a physiologic alteration of a given lesion must be coded separately; thus - acute staphylococcic pneumonia with acidosis is acute pneumonia (T and M) staphylococcus (E), acidosis (F).

Furthermore, only one morphologic complication was coded to a disease process; thus - ruptured duodenal ulcer with hemorrhage and peritonitis is duodenal ulcer with rupture (T and M) duodenal ulcer with hemorrhage (T and M) peritonitis (T and M).

Creating a Nomenclature

In addition to a classification and a coding system, an attempt was made to create a nomenclature. Granted, an international agreement on medical terms and their meanings is eventually imperative. Witness the twenty year practically unsuccessful struggle of the International Union Against Cancer to arrive at preferred names of the neoplasms. A common language acceptable to nearly all races and nations is a certainty given sufficient time.

In SNOP a preferred term receives first listing while synonyms are placed below and inset thus:

8483 Mucinous adenocarcinoma
Mucinous carcinoma
Colloid carcinoma
Colloid adenocarcinoma
Gelatinous carcinoma
Gelatinous adenocarcinoma

This is considered the scientific and logical method of arriving at general agreement on obsolescence. That is when the term has fallen into disuse, it is eliminated and does not hang around forever. In reverse, a new term can be added as a synonym if it becomes generally accepted.

Structuring the Computer

This type of nomenclature has a fundamental practical value for structuring the computer. Once it has been "taught" the preferred terms and their synonyms it can store them under one code number and on retrieval it will print out the preferred term. Since 25 percent of the 22,428 entries in the alphabetic indices of SNOP are synonyms one can easily see why an unstructured computer system such as that of Chandler-Smith could hardly be expected to properly retrieve its input especially with the conflicting individuality of several physicians. On the other hand unstructured natural language systems will accept practically anything you wish to store. There will be more on this subject later.

History of the Construction of SNOP

For those mathematically inclined, this thesis has necessitated a recent review of 72 inches of those communications which were saved and not relegated to the wastebasket. Stacked one sheet upon the next these sheets run 200 to the inch for a grand total of 14,400. Each letter has an average of 30 typewritten lines, but then I didn't read every line or page.

The original Committee on Nomenclature and Classification of Diseases, in spite of its distinguished membership, had not accomplished much in five years. Frank Queen, the Chairman, explained that there were no funds available. In late 1957 a series of letters concerning action resulted in the resignation of all but one member. A newly appointed group communicated their original ideas by mail. All felt that additions to or a separate section of SNDO was indicated. A large number of classifications were collected from institutions throughout the country.

First Meeting of Committee

The first meeting of the committee was held in June of 1958 at the new AFIP building in Washington. Here the futility of using SNDO was agreed to by all. A good beginning on a classification of morphologic alterations was accomplished. Once a skeleton classification was agreed upon a division of the work of collecting the entities was easy.

Subcommittees and Grants

Subcommittees established groups and individual entries with code numbers within the larger fields and sections. By 1959 the American Cancer Society, Inc. (ACS) agreed to provide the assistance of its statistical and computer departments to the effort with the invaluable assistance of E. Cuyler Hammond and his assistant, Mrs. Constance Percy. In September of 1960 we received a research grant from the National Institutes of Health of approximately $50,000 a year for three years. After this there were committee meetings every two months with intervening subcommittee meetings. Frequently disagreements led to heated arguments. There are twenty rejected classifications of the field of Topography in the files.

Enlarged Committee

By 1961 the committee was enlarged by five pathologists with special interest in the various disciplines of clinical pathology. They completed the field of Function. Of all the contributors in and out of the committee, the work of Sheldon C. Sommers and Louis B. Thomas was exceptional, especially the weeks spent compiling the returns from the field trial and editing the first edition.

Field Trial Edition and Its Visual Aid

Three hundred and fifty pathologists volunteered to use SNOP in their own laboratories for one year and report back their experience. The reports covered a quarter of a million surgical specimens and 6,000 autopsies. Ninety-four percent were pleased with SNOP and decided to use it in their laboratories. Over 500 other copies had been sent to selected pathologists and record librarians. Great numbers of suggestions, omissions and corrections were thus accumulated for processing. The many praises of the work were encouraging.

The need for a compendium with 95 percent of the more common diagnoses made in a pathology service of a general hospital was recognized. This was accomplished separately with the aid of 265 pathologists. This publication reduced the time of locating code numbers to a few seconds in the experience of most of the volunteers. Seventy-four percent felt that it was "useful" or "very useful." A few stated that it made the difference between using or discarding SNOP in their financially embarrassed laboratories.

CIOMS, WHO, ICD and ICDA

The urgent need for international agreement on medical nomenclature led the committee to a long series of lectures and exhibits in foreign countries. These were held at international pathology society meetings in Zurich and Moscow in 1962, Mexico City and San Salvador in 1963, London in 1964, Kyoto and Leyden in 1966, and Toulouse in 1967. It was necessary to turn down other requests for presentations because of lack of personal funds among committee members.

The Council on International Organizations of Medical Sciences (CIOMS) is composed of all international societies of the medical sciences except public health which is represented by the World Health Organization (WHO). CIOMS called a meeting of representatives of its ten international societies of the disciplines of anatomic and clinical pathology in Brussels in October 1965. After considerable discussion the representatives present unanimously approved a program for devloping an international nomenclature and code based on SNOP. The executive committee and later in 1968 in Paris, the General Assembly approved this with the stipulation that the pathologists' groups should develop and try out their fields of interest before the other specialties were involved in a Systematized Nomenclature of Medicine (SNOMed).

SNOMed

William McMenemey, neuropathologist of London was appointed chairman of the project. He started to organize his committee. A. P. Messerli, executive secretary of CIOMS sent a list of the international societies of pathology requesting a division of the pages of SNOP according to the areas of interest of the various societies. Suddenly Messerli was replaced in his position. Shortly thereafter McMenemey wrote that he could not get funds to proceed with meetings for his assignment.

It happens that CIOMS can barely exist on the dues of its members. WHO and UNESCO routinely provide funds for special projects which they must approve. WHO has a classification and coding system, the International Classsification of Diseases[5] (ICD). This publication is a most extensive collection of terms in clinical medicine including most of the specialties. It has been accepted and used successfully by the prin-

cipal health departments of the world for the statistical analysis of causes of death. WHO offered CIOMS financial aid to develop an International Nomenclature of Diseases (IND). A. G. T. Robb-Smith, Oxford professor of pathology and long-standing consultant in the development of ICD, was to become the chairman of this endeavor.

In his letters, Robb-Smith described SNOP with an obviously fixed mind and in an authoritative style. He insisted that Chandler-Smith's Natural Language computer storage system would cover the needs of pathology. Furthermore, there was nothing wrong with ICD as a storage and retrieval vehicle. Following a committee meeting in Florence, Italy, he proceeded to develop IND in the tradition of the Nomenclature of Disease of the Royal College of Physicians of London (1869 to 1957-7th ed.) In its prepublication "Computerized Drafts," it is a random collection of slightly over 1.000 morphological, functional and etiological terms with about 300 definitions and no code. Less than five percent of terms in the disciplines of medicine appear in the original trial publication. The book will be a badly needed and an important landmark when published. If it should ever cover the field of medical science and have an acceptable classification and code it would soon be in daily use in medical institutions throughout the modern world.

Since ICDA (Adapted)[6] the United States version of ICD has replaced SNDO in 90 percent of the hospitals in this country. A brief evaluation of both is indicated. ICD and its offspring ICDA had their basis of origin in the 1800's, originally designed for collecting public health statistics. Since 1949, there has been an all-out effort to add diagnostic terms from most fields of clinical medicine. The overloaded single four-digit field spilled out into "E", "N" and "Y" fields.

Briefly, if a neurosurgeon or pathologist wished a pinpoint storage of a case of meningioma in the corpus collosum or a tuberculoma in the left internal capsule it would be out of the question using the ICDs. If one wished to store the name of a single organism of a large unlisted group of bacteria or viruses it must be filed with "other bacteria." If the disease is in most specific sites of the body it must be filed as "other sites." The great majority of non-fatal diseases occur in groups with a single code number, thus the computer cannot print out a large percent of the single disease entities. The magnificent collection of diagnoses in ICD and ICDA must be restructured to meet the requirements of today's mechanical technology.

Computer Age

This is the computer age. Physicians must utilize this mechanical brain much more than they have to date. The computer can be trained or "structured" to store complete classifications with codes so that one need not code diagnoses to store them. The simply typed or spoken disease name or any of its synonyms will be stored and retrieved. Thus using SNOP one can retrieve complete discharge notes on patients including history, physical findings, symptoms, diagnoses, autopsy findings and eventually therapy, possibly using CPT of the AMA. Groups of patients with any single one of the listed features recorded may be retrieved. Eventually diagnostic and therapeutic aids will be available along with many other uses.

Selected Highlights of SNOP's Reception

Seminars, workshops, lectures and exhibits have been conducted annually at CAP-ASCP meetings in Chicago, New York, Miami and Seattle. Nine thousand copies of SNOP have been sold throughout much of the world. At the last of the workshops in Chicago, George E. Gantner, associate professor, medical examiner and computer expert of St. Louis, presented his publication, "Data Processing Methods for Diagnostic Codes—Systematized Nomenclature of Pathology." It covers the many uses of SNOP and is available at the CAP office at a nominal price. Recently Doctor Gantner has developed an Automatic Autopsy Protocol for Computer and a Compendium for Forensic Pathology using SNOP code. The former can completely replace the use of a medical secretary.

Virgil Slee of the Commission on Professional and Hospital Activities of Ann Arbor accepted SNOP on their computer to store pathologists' records from hundreds of hospitals throughout the country. The National Heart and Lung Institute of the Public Health Service and the International Society of Cardiology utilized SNOP code in their classifications.[7,8]

Within two months of our exhibit in Kyoto with the assistance of John W. Berg of the Na-

tional Cancer Institute, the Japanese pathologists were given permission to translate SNOP to Japanese using the SNOP code. They had finished the translation a year later and were storing all autopsy diagnoses from all parts of the nation on a computer in Tokyo.

Ronald S. Beckett, chief pathologist of the large (900 bed) Hartford General Hospital working with the chief record librarian, Jean A. Ryan, RRL, has published articles[9] and given lectures on the use of SNOP for record room computer storage of diagnoses in all specialties of medicine. They claim great success in using SNOP for three years and 300,000 discharge diagnoses using some 800 additional new terms for the entire field of clinical medicine. This work has led Roger Cote on the Faculty of Medicine at the University of Sherbrooke to translate SNOP into French and use it for central computer storage of general hospital records for 18 hospitals in Quebec.

Eric P. van der Esch of Wilhelmia Gasthuis, University of Amsterdam, writes that the pathologists of Holland have financed a project PALGA. This will translate the English of SNOP into the Dutch and Latin languages. This is planned to result in central computer storage of all autopsies performed in Holland when it is finished.

Following a recommendation to the publishing company by Professor H. Hemperl, Head of the Department of Pathology of the University of Venusberg in Bonn, to the publishing company, Springer-Verlag requested permission in 1968 to publish SNOP as a book in four languages—English, German, French and Italian. The Board of Governors of CAP, contrary to the wishes of the committee, refused to permit the use of English. The publisher dropped the project.

In the Department of Anatomical Pathology of the National Institutes of Health, Louis B. Thomas computerized 200,000 diagnostic terms from autopsies performed over the previous ten years. He experienced excellent retrieval of diagnostic information. Later with the assistance of Arnold Pratt, hospital discharge notes on patients' charts were computerized with success.

Of all the uses of SNOP, undoubtedly the most productive was that of Arnold W. Pratt, Director of Computer Research and Technology at the National Institutes of Health. Using SNOP and assisted by his staff of linguists over the past six years he has promoted the computerization of medicine more than any one individual. He has revealed the amazing complexity of the natural language of medicine as used by highly trained physicians.[10] The computer must be structured to receive these numerous expressions as synonyms of preferred terms. This new science of Computational Linguistics reached a peak of practical accomplishment with the machine translation from Russian into English. This work is referred to as the "IBM-Georgetown Experiment." It was recognized that the computer which has the capacity to handle symbols effectively can also treat words as symbols and language as a string of symbols. The jargon of this science is guaranteed to lose the uninitiated in seconds. For one thing, linguistic analysis reveals a mixture of Latin, Greek and English suffixes and prefixes are used frequently and interchangeably. There is also a heterogeneous linguistic origin found in single word forms and a veritable jumble of compound word forms used routinely by physicians. A few examples will illustrate this:

Semantically Equivalent Phrases

muscle atrophy
atrophy of muscle
atrophic muscle
muscular atrophy

parathyroid gland adenoma
parathyroid adenoma

congenital aortic stenosis
congenital stenosis of aorta

acute staphylococcus pneumonia
acute pneumonia due to staphylococcus

It becomes abundantly apparent that a natural language classification of medical terms is much more complicated than it was before January of 1965 when SNOP was written. Numerous synonyms must be added in all fields. Suffixes and prefixes may need inclusion. When this and more is accomplished, the computational linguists will be needed to structure the computer to automatically handle the language we unconsciously scramble.

Contacts with the American Medical Association have been continuous from the first meeting at the AFIP in 1958 when Mrs. Adelaide Hayden, Asst. Editor of SNDO was present. We assisted Burgess Gordon with his editing of the pathology

aspects of CMT. After a series of meetings in November 1964, Hugh H. Hussey, director of scientific activities of the AMA offered to store SNOP on their computer with the prospect of making additions and eventually automatically print out the second edition of SNOP on the computer which prints the JAMA and other journals. Unbeknown to the committee this was never accomplished. At present the matter of preparing a master nomenclature and code of clinical medicine using the assistance of the various national specialty societies is pending in the House of Delegates. The AMA is unquestionably the natural owner of a SNOMed—a computer language of medicine. The task of seeking out the terms for this publication can be accomplished without much difficulty from the extensive publications of the various specialties. How to get authoritative approval of the nomenclature and properly classify the terms will be more difficult.

Summary

I would like to end my presentation with a listing of the unique structure and exclusive features to be found in SNOMed. You can compare them with those of the ICDs, SNDO, CMIT and others. They include:

1. A classification and coding system of medical terms into their "medical parts of speech," i.e., Site, Morphology, Etiology, Physiology, Therapy and Diagnostic Procedures in the style found in SNOP.
2. A classification and code for practically all terms in all specialties of medicine for their routine clinical practice for a single central storage and retrieval department.
3. Numerical equivalents with equal recognition of each disease entity (mild or fatal), each anatomic site, each named morphologic change, each altered function and insofar as is practical each etiologic agent.
4. A hierarchal classification and code using the decimal system permits a flexible contraction of any part of the detailed lexicon.
5. The use of well organized and constructed compendiums that assist the general hospital as well as specialty institutions with an almost instantaneous code for 95 percent of their diagnoses.
6. There will be a coded classification of every anatomic site of practical importance to each of the various specialties of medicine.
7. The expert guidance and assistance of Arnold Pratt, M.D. and his computational linguists of Computer Research and Technology of NIH, plus his encoding instructions for the use of SNOP.
8. Probably the only complete single source of internationally (IND of CIOMS) and nationally (CMIT of AMA) approved preferred nomenclature at the time of publication.
9. The capability of receiving printouts of any requested set of clinical information from a computer encoded with the numerical indexes of SNOMed and the instructions of computational linguists with simple natural language storage (typing) eliminating hand coding.

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But most thro' midnight streets I hear
How the youthful Harlot's curse
Blasts the new born Infant's tear,
And blights with plagues the Marriage hearse.*

*William Blake: London.

Legislation

Interim Committees Focus on Health Issues

THE COMMITTEE SYSTEM is the legislature's way of delegating responsibility and maintaining a continuous, smooth functioning operation in the face of manifold and complex problems. Not all legislative responsibility can be efficiently carried out by a legislative body acting as a whole nor can all issues be given in depth consideration during the 120 day regular biennial sessions. This has given rise to Permanent, Interim and Standing Committees. Standing Committees function through each legislative session. Permanent Committees and Commissions, as distinguished from those operating only during sessions or the interim between sessions, are established to deal with problems of a continuous and recurring nature.

Interim Committees and Commissions are designed to operate during the period between regular sessions of the legislature. Many Standing Committees are also activated during the interim period. These committees investigate and study various programs and policies which are expected to be the subject of legislation in the next session. Committees and subcommittees studying a variety of state concerns will be reporting their findings and making recommendations to the 1973 Legislature based on information obtained since the 1971 session.

This interim period has been shortened considerably by the length of the special session last year. However, several committees have been studying numerous health or medically related matters of importance to medicine during this period. This is not surprising as there were well over 300 health related bills introduced and considered by the 1971 Legislature. Attracting much public attention this year were interim hearings of a special House Subcommittee on Nursing Homes during which extensive testimony, both pro and con, was given regarding the quality of care in Minnesota nursing homes. This committee, chaired by Representative Gary Flakne of Minneapolis, also has been conducting on-site inspections of certain nursing homes to attempt to evaluate the need for special legislation in 1973. The Minnesota State Medical Association has assisted this committee by arranging for physicians, primarily from the MSMA Committee on Aging, to accompany the committee on their inspection tours. The Medical Education Subcommittee of the House Appropriation Committee has been especially active this interim. As medical education was heavily funded by the 1971 Legislature, progress reports are being made to this committee by administrators and directors of the various graduate and undergraduate programs in medical education. Presentations have been made to the committee regarding the new two-year Medical School at the University of Minnesota, Duluth, the newly funded four-year Medical School at Mayo, the expanded Medical School program at the U of M, and various graduate and undergraduate hospital based programs. The committee has been keenly interested in learning of the progress made in the training of family practitioners as these programs were given top priority last session. Committee members have generally reacted favorably to the progress reports given to date.

The Medical Education Committee has also scheduled hearings to study the adequacy or need for funding of nursing and other allied health education programs.

A special charge given the House Medical Education Subcommittee this interim was to attempt to resolve the interdisciplinary problems which arose last session over MSMA's Delegatory Bill and Comprehensive Health Planning proposal to certify allied health manpower through a health manpower commission.

The Health Subcommittee of the House Health Welfare and Corrections Committee has met a number of times this interim to discuss such matters as health maintenance organizations, comprehensive health planning, the State Board of Health, certification of need legislation and various other matters relating to health delivery. Governmental reorganization of the occupational and professional licensing boards has been the subject of much staff research and committee deliberation, especially on the Senate side of the Capitol.

The Senate Civil Administration Subcommittee on Health Services and Consumer Affairs and the Senate Committee on Health and Welfare have listened to departmental and research staff presentations suggesting an overhaul of the independent licensing board structure especially in the area of the health professions. Legislation may be recommended for 1973 by these interim committees calling for consumer representation, central housing

and administrative services for the licensing boards and possibly a superboard which would license all the health professions.

The activities and organization of the State Board of Health have also come into sharp focus during this interim period. Dr. Warren Lawson, Executive Secretary of the State Board of Health, has presented detailed testimony to interim committees on more than one occasion. Historically a target for governmental reorganization, the State Board of Health has been provided ample opportunity in the interim hearings to advise the legislators of its activities and operations.

Also of interest to medicine is a special Subcommittee on Alcohol and Drug Laws of the House Judiciary Committee which is considering the advisability of recodification of the numerous State laws relating to alcohol and drugs. Input from the MSMA Subcommittee on Alcoholism and Drug Abuse will be made before this interim committee formulates its recommendations. A Subcommittee of the Senate Judiciary Committee is considering a proposal for a new professional corporation act to replace the separate acts now existing for each separate profession including medicine.

In the area of welfare the 1971 Legislature charged the Commissioner of Public Welfare with developing a comprehensive plan for the future use of State institutions, to make recommendations regarding community based programs and generally to review and revamp Department of Public Welfare programs relating to mental illness, retardation and inebriety. As a result of this charge Welfare Subcommittees in both the Senate and House have been appraised of progress in this area by personnel from the Department of Public Welfare. A final plan will presumably be forthcoming this year.

Coming under close scrutiny by legislative interim committees in the Senate and House is the welfare appropriation for medical assistance. While testimony on nursing home rates have monopolized much of the committees' time, other components of the medical assistance dollar have also been discussed including proposals to curb presumed overutilization of medical services.

The aforementioned areas of interest to medicine are by no means inclusive of all the health related subjects coming under the purview of the interim committees during this seemingly brief interval between sessions. It should be apparent to the reader though that the legislative responsibility of the MSMA is an on-going one which does not end with each session's adjournment. Interim committee hearings are audited regularly by MSMA representatives and appropriate testimony given when indicated. The legislative proposals embodied in these interim committee reports are obviously only recommendations. Often these interim reports fail to see the light of a legislative day particularly if its interim advocate(s) are not reelected. Chances are though that most interim recommendations will be considered by some legislators to be worthy of introduction in bill form making it all the more important for medicine to assist and participate in the legislative process between, as well as during, each session.

A Strange Language

A Lawless Language is English:
The plural of box is boxes,
But more than one ox is not oxes.
One fowl's a goose, more are two geese,
But more than one mouse is certainly not meece.
On the contrary for mouse, the plural is mice,
While the plural for house is never hice!
If more than one man is always men,
The plural of pan should then be pen?
One may be that and two may be those,
But the plural of hat is surely not hose!
Masculine pronouns are he, his and him.
Imagine the feminines she, shis and shim!
The English language, I think you'll agree,
Is as strange a language as ever could be.

140/90 is normal blood pressure...or is it?

An extensive study based on nearly 4 million life insurance policies suggests that a blood pressure reading of 140/90 requires close medical supervision.

Study Findings. Twelve years ago the Society of Actuaries reported on an extensive study based on the lives and deaths represented by almost 1 million life insurance policies. From this vast survey—"The Build and Blood Pressure Study"[1]—insurance experts concluded that:

Blood pressure above 140/90 is accompanied by increased morbidity and requires close medical attention.

Even small increments in either systolic or diastolic blood pressure progressively and steeply shorten life expectancy.

Other Studies. Studies conducted with large numbers of patients since that time have echoed the above findings. Two studies published in 1970—the VA Cooperative Study Group on "Effects of Treatment on Morbidity in Hypertension"[2] and the "Framingham Study"[3]—suggest that treatment of even mild hypertension may, over time, offer significant benefits to the patient.

Another Point of View. Although a growing body of studies suggests that treatment of mild hypertension is warranted, medical opinion is not unanimous. Some clinicians recommend that drug treatment for mild hypertension be reserved for patients with additional risk factors such as smoking, high cholesterol



levels, heart or kidney involvement, or a family history of vascular disease. Dr. Walter M. Kirkendall stated this position in his recent paper "What's With Hypertension These Days?"[4] Discussing the management of hypertension in patients with a sustained diastolic pressure up to 100 mm Hg, he said: "Generally, I do not recommend antihypertensive therapy unless patient's blood pressure approaches the upper limit for the group and a number of adverse factors exist, such as male sex, family history of vascular disease, youth, evidence of heart or kidney involvement."

Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

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Therapy to Start With

For a brief summary of prescribing information, please see next page.

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Therapy to Start With

Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to this compound. Nursing mothers; if use of drug is deemed essential, patient should stop nursing.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function to avoid cumulative or toxic effects. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis.

When used with other antihypertensive drugs, careful observation for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents, especially ganglion blockers, must be reduced by at least 50% because HydroDIURIL potentiates their action.

Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery was frequently required, and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs.

Thiazides cross placenta and appear in cord blood. In women of childbearing age, potential benefits must be weighed against possible hazards to fetus, such as fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives, including thiazides.

PRECAUTIONS: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive or patient is receiving parenteral fluids. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop (especially with brisk diuresis) in severe cirrhosis; with concomitant steroid or ACTH therapy; or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypokalemia may be avoided r treated by use of potassium chloride or giving fo with a high potassium content. Similarly, any chlor deficit may be corrected by use of ammonium chlor (except in patients with hepatic disease) and larg prevented by a near normal salt intake. Hypochlorer alkalosis occurs infrequently and is rarely severe. severely edematous patients with congestive failure renal disease, a low salt syndrome may occur if diet salt is unduly restricted, especially during hot weath

Thiazides may increase responsiveness to tubo rarine. The antihypertensive effect of the drug may enhanced in the postsympathectomy patient. Arte responsiveness to norepinephrine is decreased, nec sitating care in surgical patients. Discontinue drug hours before elective surgery. Orthostatic hypotensi may occur and may be potentiated by alcohol, barb urates, or narcotics.

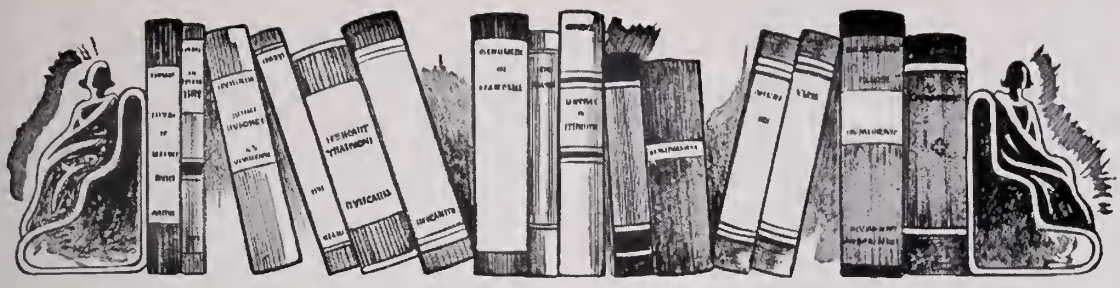
Pathological changes in the parathyroid glands w hypercalcemia and hypophosphatemia have been se in a few patients on prolonged thiazide therapy. T effect of discontinuing thiazide therapy on serum c cium and phosphorus levels may be helpful in asse ing the need for parathyroid surgery in such patier Parathyroidectomy has elicited subjective clinical i provement in most patients, but has no effect hypertension. Thiazide therapy may be resumed af surgery.

Use cautiously in hyperuricemic or gouty patien gout may be precipitated. May affect insulin requi ments in diabetics; may induce hyperglycemia a glycosuria in latent diabetics.

ADVERSE REACTIONS: Rare reactions inclu thrombocytopenia, leukopenia, agranulocytosis, apl tic anemia, cholestasis, and pericholangiolitic hepatit Nausea, vomiting, diarrhea, dizziness, vertigo, par thesias, transient blurred vision, sialadenitis, purpu rash, urticaria, photosensitivity, or other hypersen tivity reactions may occur. Cutaneous vasculitis p cipitated by thiazide diuretics has been reported elderly patients on repeated and continuing expos to several drugs. Scattered reports have link thiazides to pancreatitis, xanthopsia, neonatal thro bocytopenia, and neonatal jaundice. When adve reactions are moderate or severe, the dosage thiazides should be reduced or therapy withdraw

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Book Reviews

CURRENT DIAGNOSIS AND TREATMENT, 1972. Krupp, M.A., and Chatton, M. J. Lange Medical Publications, Los Altos, Ca., 1972. 962 pages. Paper back $11.00.

This work was first published in 1962 with re-issue of copyrights and presumably new editions approximately yearly. The first item of business perusing a re-issue is to determine whether the recent copyright, 1971, and the 1972 on the cover indicate that the material is updated. There are indeed many references to 1970 and 1971 publications indicating immediacy of the material. I prefer to see the references keyed specifically to statements instead of being simply listed generally at the end of chapters. The sections fulfill the purpose of a textbook in medicine outlining the important features of disease, their diagnosis and treatment, and listing significant references for further reading. There are 34 collaborators mostly from the faculties of Stanford and San Francisco.

Reuben Berman, M.D.
Minneapolis, Minnesota

PEDIATRIC THERAPY, 4th Edition. H. C. Shirkey, Editor, C. V. Mosby Company, Saint Louis, 1972, $34.50.

This volume is a welcome review of the 1968 date line 3rd Edition. It stands to become as useful to the family practitioner and pediatrician as the Bible is to the clergyman.

This formidable compendium by todays experts on their recommendations for specific therapy for specific disease deserves consultation when an unfamiliar disease problem occurs in a pediatric patient.

This book will also provide a useful consultation regarding therapy for familiar conditions to discover better ways to approach an old problem or confirm a present regular prescription. *Pediatric Therapy,* 4th Edition is a recommended best buy.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

INSTRUCTIONAL COURSE LECTURES. The American Academy of Orthopedic Surgeons. Vol. xx, 1971. Publishers: C. V. Mosby Co., St. Louis, Missouri.

As in past volumes, the 1971 *Instructional Course Lectures* provides an excellent review of selected topics related to orthopedic surgery by leading authorities.

Especially well done are sections dealing with cerebral palsy, with particular emphasis on the lower extremity, and the discussion of intertrochanteric osteotomy of the hip for degenerative joint disease by Karl H. Mueller.

Other fine contributions include surgical anatomy of the knee and a section on lower extremity bracing. Arthur J. Helfet has written a section which nicely describes the early changes of osteoarthritis of the knee. The author's discussion of surgery for this condition is quite superficial and should be better covered in future volumes.

The use of medullary fixation as a primary treatment in fractures of forearm bones is recommended in a section written by Fred T. Sage. However the use of compression plate fixation for most of these fractures appears to be gaining wider acceptance as results of treatment are accumulated.

This is an excellent volume on many timely subjects and is recommended for all of those interested in orthopedics.

Lee C. Detenbeck, M.D.
Rochester, Minnesota

APPROACH TO THE MEDICAL CARE OF THE SICK NEWBORN, by Sophie H. Pierog, M.D., and Angelo Ferrara, M.D., the C. V. Mosby Company, St. Louis, 1971: 292 pages; Price $11.50.

The subspecialty of pediatricts called *neonatology* is so new that it is peopled almost entirely by physicians who have learned from each other and from their own experiences. What they have learned in the last decade they are now teaching to tomorrow's innovators in a few major centers. Most of the information needed for the care of the sick newborn thus is available only in the pages of scattered journals, limited circulation manuals for nurses and residents and in the minds of the neonatologists themselves.

Into this little book, two obviously experienced and thoughtful pediatricians have poured a great deal of valuable information. The material is presented in short, pithy chapters in which good use is made of charts, flow diagrams, tables, and well organized prose. Line drawings are used to advantage as chapter headings and to illustrate such diverse subjects as gestational age and prevention of maternal Rh sensitization.

The book opens with a short initial section on the organization of newborn services and closes with a series of appendices which include details on procedures (such as umbilical vessel cannulation and blood sampling microtechniques) infant drug dosages, formula contents, and normal laboratory values. The rest of the book covers in a concise, readable way most of the problems—physical, physiological, sociological, and economic—that the physician, the infant, the infant's parents, and the community have to face.

This book should be of value to pediatric and obstetric residents and to nursing personnel in newborn intensive care units. More important, however, would be its availability to any physician who cares for newborns in the community hospital away from a specialized neonatal care unit. Two evenings spent perusing these pages will pay off in better care for the normal newborn and greater salvage of the sick newborn whether transferred to a specialized center or not.

Charles W. Jarvis, M.D.
St. Paul, Minnesota

Hexachlorophene Merry-Go-Round

The U.S. Food and Drug Administration is developing reservations concerning the safety of hexachlorophene following reports that untoward results have been observed in rats and monkeys previously exposed to the drug in abnormally large quantities.

Such reports should be interpreted with great caution. In the case of the experimental rats the animals were fed hexachlorophene. No one has ever recommended the oral route for human beings. In the case of the baby monkeys, one authority estimates that from four to six times greater amounts were used than is customary for humans.

The FDA, in announcing restrictions on the use of hexachlorophene, stated that there has been no evidence of harm to humans when it is used as recommended. One of the standard cautions has been for careful clear water rinsing after bathing.

The head of the Canadian Health Department Food and Drug Directorate said that the bacteria-destroying chemical has been used without ill effect for more than 20 years to bathe newborn infants. Other than advising physicians to ensure careful compliance with instructions for proper use the Canadian said further that his committee would monitor further developments and would not change policy until results of experiments were known.

The backlash effect in the United States is already evident. There are reports of nurseries wherein epidemics of staphylococcal skin disease have developed following discontinuance of hexachlorophene bathing.

It doesn't take a very long memory to go back to prehexachlorophene days when such epidemics were stubborn and dangerous—sometimes being associated with fatalities.

Further animal experimental studies are being done. In view of the fact that no human toxicity under normal use conditions has ever been reported it would seem to be wise to await the additional information which will be provided.

March 1972 issue, Indiana Med. Assn. Permission to copy granted by Frank B. Ramsey, M.D.

Calm as a clock your knowing hand directs,
Rhei, jalapae ana grana sex,
Or trace on some tender missive's back,
Scrupulos duos pulveris ipecac;
And leaves your patient to his qualms and gripes,
Cool as a sportsman banging at his snipes.
But change the tune, the person, and the place,
And be yourself "the interesting case,"
You'll gain some knowledge which it's well to learn;
In future practice it may serve your turn.
Leeches, for instance—pleasing creatures quite;
Try them—and bless you—don't you find they bite?*

*Oliver Wendell Holmes, Sr.: The Morning Visit, 1849.

Classified Advertisements

Classified advertising rates are thirty (30) cents a word; minimum monthly charge $7.50; key number, fifty (50) cents additional.

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ASSOCIATES WANTED: Family doctors to join a growing Family Practice Department in a large multiple specialty medical center, Minneapolis suburb. Excellent opportunity for teaching undergraduate and graduate students in Family Practice. Four man department with excellent growth potential. Reply to Dr. Harley J. Racer, Chairman Family Practice Department, St. Louis Park Medical Center, St. Louis Park, MN 55416. Telephone 612-927-3320.

GENERAL PRACTITIONER to join young 5 man family practice group. College town of 7,000 serving approximately 20,000 population. Accredited hospital with specialist consulting staff. 30 miles from St. Paul-Minneapolis, Minnesota. Contact R. M. Hammer, M.D., River Falls Medical Clinic, River Falls, Wisconsin 54022. Phone (715) 425-5322.

GENERAL PRACTITIONER needed for an extremely busy rural practice in Northern Minnesota. Excellent hospital and clinic facilities. Starting salary of $25,000.00 with possible early partnership. Write MINNESOTA MEDICINE, Box 466, 375 Jackson, St. Paul, Minn.

FAMILY PHYSICIAN WANTED to take over busy well established practice in Lake Calhoun area. Fully equipped office with 100 MA x-ray, lab. and operating rooms. This is an especially good opportunity for one or two Physicians. Will introduce clientele. We also service many Nursing Home Patients. John J. Pone, M.D. 1620 West 32nd Street, Minneapolis, Minnesota 55408. Phone: 825-0400.

INTERNIST WANTED—Thirty-five doctor prepaid multi-specialty group is opening attractive new offices. Excellent earnings and assured advancement in desirable professional environment. Many tax sheltered benefits, good community near downtown. Generous vacation, conference and teaching time. A. F. Anderegg, M.D., Group Health Plan, Inc., 2500 Como Ave., St. Paul, Minn. 55108. Phone (612) 645-5851.

GENERAL SURGEON NEEDED for well established group of 7 g.p.'s. Located in beautiful northern Minnesota community serving 15,000 people. Stable diversified economy, excellent medical facilities, year round recreation and cultural center, and extremely pleasant family environment. Starting salary open depending on training and experience, all fringes, IRS approved pension fund, and attractive buy in option after 1 year. Contact. K. H. Stolen M.D. or T. R. Brill Adm. Box L Grand Rapids, Minn. 55744 or call 218-326-6613.

(Continued on page 599)



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Join MINNPAC today. Participate in the political and governmental process which will ultimately determine how the practice of medicine will be structured during this decade. Your $25.00 includes both MINNPAC and AMPAC dues and will be used to assist in electing responsible men and women in both parties to the State Legislature and to Congress. The MINNPAC Board of Directors is charged with the responsibility of urging physicians and their wives to become actively involved in the support of candidates and the party of their choice. *YOUR* help is needed *NOW!* Complete the application form or merely send your $25.00 check to: MINNPAC, Metro Medical Building, 825 South 8th Street, Room 503, Minneapolis 55404.
P.S. Those of you who have already sent your check—*Thank You!*

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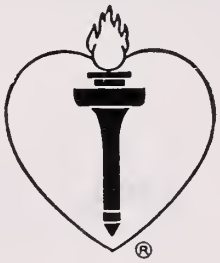
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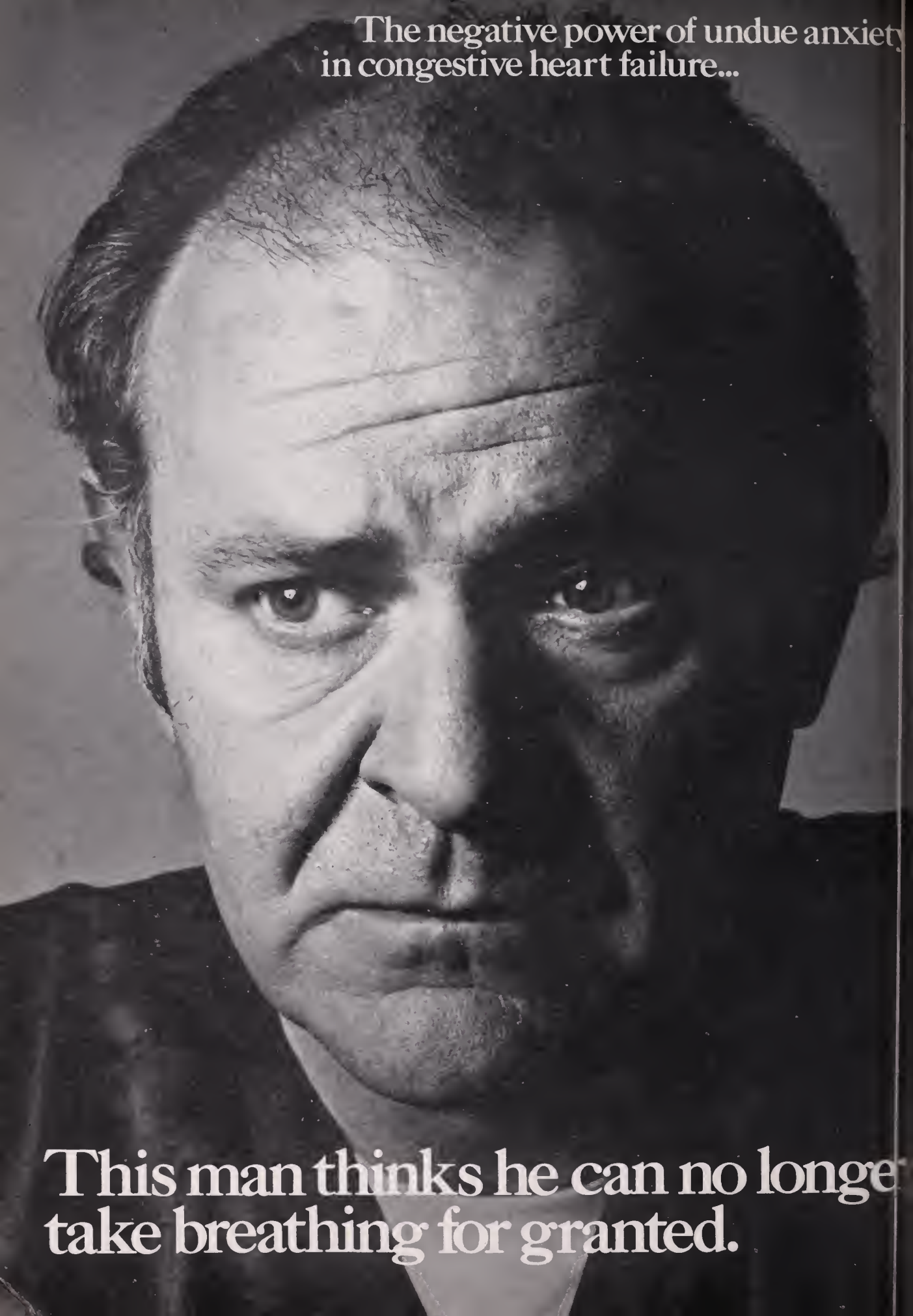
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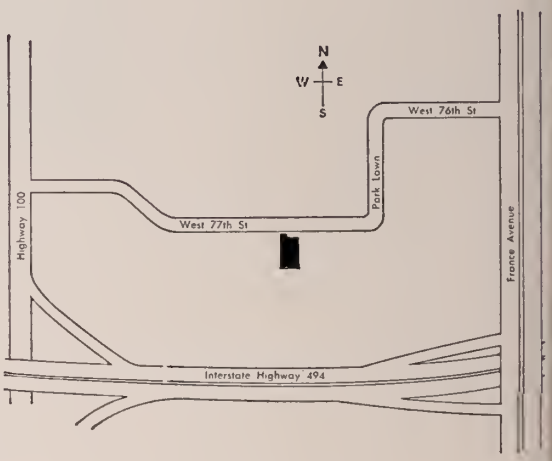
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President's Letter



Change

THE MINNESOTA STATE MEDICAL ASSOCIATION'S 119th Annual Convention has passed into history. One-fourth of our membership registered and participated in the scientific and business sessions. This is encouraging because the Minnesota State Medical Association can be representative of only those physicians who wish to express their views and can enhance the knowledge of only those who avail themselves of the opportunities to learn. Change is occurring. The scientific assembly had a new format and was well accepted. The Permanent Evaluation Committee suggested changes that the delegates implemented and is considering others. The House of Delegates has endorsed the principle of open elections and directed the formation of an Ad Hoc Abortion Study Committee, as well as directing new and renewed activity toward many of our scientific and non-scientific committees.

There was one surprise, a disappointing one. Most physicians I know feel that the AMA needs to change, but the AMA's Long Range Planning and Development Council heard only eighteen witnesses. The Council assembled its members from all corners of the nation on its own initiative, it was not directed to do so. Granted the site chosen by the AMA was removed from the main convention proceedings, the proceedings were often closer to a debate than an information gathering forum, and the original invitation was too easily interpreted as overly restrictive in what testimony would be heard, but after years in "organized medicine" and one of your delegates to the AMA, I was surprised to find so few who actually availed themselves of this opportunity to present their feelings about the AMA and what course it should follow in the future. The Council on Long Range Planning and Development should be commended for its appearance at our state meeting. Their presence denotes interest and willingness to change on the part of AMA. It is my sincere desire that you will share with your officers and councilors your feelings about the AMA *Your* AMA delegation would like to accurately represent you at future national conventions.

Two more changes. First, kudos for outstanding performance during his year as president to my dear friend, Robert T. Kelly. Peace and more time for your family, Bob. Secondly a welcome to John J. Regan, president-elect. I look forward to our association in the coming years.

George B. Scanlan

President
Minnesota State Medical Association

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"Cholangiolitic" Hepatitis and Cirrhosis ("Primary Biliary" Cirrhosis)

A Brief Review with Special Reference to Atypical Cases

GENE HARTMANN, M.D. AND C. J. WATSON, M.D., Ph.D.*

AHRENS AND CO-WORKERS[1] in their well known paper on "primary biliary" cirrhosis, credit Murchison with the first description of a case in 1869. It is interesting that Murchison's case was listed as "alcoholic cirrhosis." Hanot in 1875 described cases of "hypertrophic cirrhosis with chronic jaundice,"[2] also emphasizing lack of ascites and frequency of pruritus. These cases were very similar clinically and in gross pathologic terms to what today is commonly called "primary biliary" cirrhosis. Xanthomatosis has often been associated with this type of cirrhosis, and for a time Thannhauser and co-workers[3] believed that intrahepatic xanthomata were the cause of an obstructive biliary cirrhosis. Yet cases in which this sequence might be assumed, are rare. Also, there have been many instances in which a primary biliary obstruction such as stone, stricture, or cancer, has caused development of xanthomata as a result of the secondary hyperlipemia.[1] Ahrens[1] emphasized that many cases of "primary biliary" cirrhosis have been described both with and without xanthomatosis. Recent reviews[4-6] are in accord.

Clinical Features

Although an insidious onset of jaundice and pruritus is common, there are some remarkable variations in the clinical picture. The patient may be completely asymptomatic, or complain of nothing more than itching and/or darkening (melanosis) of the skin, even without jaundice. Less commonly, fatigue, weakness, loss of weight and loose stools are the presenting complaints. Abdominal pain, at times simulating biliary colic, may occur. In exceptional cases a history of exposure to chemicals or an earlier attack of hepatitis is noted. Females are affected much more often than males, and more frequently in middle age.[1,4]

The physical findings vary with the evolution of the disease. The liver is invariably palpable, often markedly enlarged and usually not tender. Evidence of pruritus is common. Jaundice is usual but variable and xanthomata are often encountered. Quite frequently there is prominent darkening of the skin, at times constituting the patient's chief complaint. This is generally believed to represent a melanosis,[1] though it has not been explained. Spider nevi are usually not as prominent as in Laennec's cirrhosis.

Laboratory Findings

Of the laboratory findings the most consistent and at times the only abnormality is an elevated serum alkaline phosphatase. When pruritus is present this is accompanied by marked increases of serum bile acids, particularly the trihydroxycholanic type.[7] The serum cholesterol,[4,8] mainly the esterified fraction, as well as phospholipids and total lipids[9] are characteristically increased and the greater the increase the more likely the appearance of xanthomata. The α_2[9] and β globulins[4] are likewise increased with the hyperlipidemia. Highly significant increases of IgM and antimitochondrial antibodies are rather characteristic.[9-11] The serum albumin usually remains at a relatively normal level for years. This together with the increased serum cholesterol bespeaks a relatively normal hepatocellular function. Late in the course of the disease, often only after years of chronic jaundice and pruritus, hepatocellular function fails progressively and the clinical picture may then resemble a more ordinary type of cirrhosis. In this late stage ascites may appear,

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Address for proofs: Dr. C. J. Watson, Northwestern Hospital, Minneapolis, Minnesota 55407.

but even in its absence esophageal varices may bleed and cause death.

Terminology and Pathologic Classification

The designation "primary biliary" cirrhosis was introduced by Dauphinee and Sinclair in 1949[12] and championed in the following year by Ahrens and co-workers.[1] Though widely used, the term has not been acceptable to many students of liver disease, as cirrhosis is preceded by a protracted form of hepatitis. Other designations include "chronic nonsuppurative destructive cholangitis,"[13] "chronic intrahepatic obstructive jaundice,"[5] "nonobstructive cholangitic biliary cirrhosis,"[14] "chronic intrahepatic obliterating cholangitis,"[15] and "cholangiolotic"[16] or "cholangiotoxic" cirrhosis.[16] The term "pericholangiolitic" has also been used.[6,18,19] Injury, destruction or lysis of the smaller biliary channels are suggested in these terms. They were implicit in the designation "cholangiolitic" as used in 1946 by Watson and Hoffbauer,[17] for this form of cirrhosis, as well as its preceding hepatitis. The term "cholangiole" is used arbitrarily to include the ampullae of the bile capillaries (canal of Hering) as well as primary and interlobular bile ductules. At the time of their description, Watson and Hoffbauer[17] were more concerned with functional than anatomic considerations and the lack of definite histologic criteria no doubt accounts for failure of the term "cholangiolitic" to gain more widespread acceptance. Rössle[16] had used the term "cholangiolotic" for such cases, possibly in analogy with "nephrotic," to avoid implication of an inflammatory in contrast with a metabolic process. However, the term "cholangiolitic" appears justified in view of the evidence of a preliminary hepatitis (portal cellular exudate), the marked cholangiolysis and the disappearance of cholangioles. The term was later validated in the recognition by MacMahon[18,19] and others[4,6,13,20] that cholangiolysis is characteristic and evidently a basic phenomenon of the disease together with the clear evidence of chronic hepatitis which precedes the cirrhosis. The early abnormality and progressive disappearance of primary bile ducts in the portal spaces has become widely accepted as a histologic criterion for the diagnosis of "cholangiolitic" or "primary biliary" cirrhosis.

Case Reports

We have recently studied two cases* with the histologic diagnosis of hepatitis and cirrhosis ("primary biliary" cirrhosis). Their chemical and immunologic findings were quite atypical.

Case 1

A 70-year-old white female was first seen on August 11, 1970, with nausea, vomiting, and right lower abdominal pain radiating to the right flank. Her past history included cholelithiasis and mild episodes of cholecystitis. There had been no jaundice or pruritus. Physicial examination revealed a number of spider nevi and hepatosplenomegaly. The patient underwent a laparotomy for bowel adhesions. The liver was noted to be large and diffusely nodular. The patient was discharged after a few days but readmitted on November 29, 1970 for failure to regain strength. On December 11, 1970, a second laparotomy was done to determine the status of her biliary tract. The gallbladder was

*We are grateful to the attending physicians, Drs. Robert Scott and James Myhre, for permission to report Cases 1 and 2 respectively.

TABLE 1
Essential Laboratory Data in Case 1, Female, 70, 1970-71

Serum (see Normal Range, Table 2)	8/11/70	11/30/70	1/11/71	3/16/71
Bilirubin (mg%)				
Prompt direct	0.9	0.2	1.2	0.4
Total	1.6	0.8	2.5	1.5
Cholesterol (mg%)		176	185	246
Triglycerides (mg%)				55
Bile Acids (mg%)				
Trihydroxy			2.1	
Dihydroxy			0.8	
Alkaline Phosphatase, I.U.	490	425	520	259
SGOT (units)	79	94	96	84
SGPT (units)		22	38	16
Albumin (gm%)	3.4	3.2	3.0	3.4
α_1 globulin (gm%)		0.2		
α_2 globulin (gm%)		1.4	1.4	
β globulin (gm%)		1.1		
γ globulin (gm%)		1.8		

Addition data: (1/11/71) Antimitochondrial antibody titer 1:10; (11/30/70) BSP retention 14%, 45' after after 5 mg/kilo; prothrombin time 14.2/12.1; cephalin chol. flocculation 4+; thymol turbidity 11 units; FANA, latex fixation, Australia antigen, all negative; normal amounts of IgA, IgG, and IgM, on immunoelectrophoresis.

removed. There was chronic cholecystitis and cholelithiasis. The common duct was slightly thickened but not dilated, containing several 1 mm stones. T-tube drainage was instituted and continued until January 19, 1971. A wedge biopsy of the liver, on microscopic examination (Figure 1)* revealed: (1) marked sparsity of portal biliary radicles; (2) nodular cirrhosis; (3) occasional epitheloid cell granulomas; (4) prominent portal lymphocytic exudate, and (5) evidence of mild cholestasis, i.e., bilirubin staining of cells and occasional bile thrombi. The pathologist† stated that the histologic picture, especially the evidence of cholangiolysis, was most compatible with "primary biliary cirrhosis," rather than a secondary biliary cirrhosis in which ductular proliferation is prominent. The laboratory data, as shown in Table 1, were discordant with the histologic diagnosis except for a striking increase in alkaline phosphatase. The serum bilirubin was moderately increased and remained elevated two months after the second laparotomy. The serum cholesterol, antimitochondrial antibody, and immunoglobulins were normal. The serum bile acids were normal in accord with the absence of pruritus.

*We are indebted to Dr. N. Kostich, pathologist, for the microphotographs of Figures 1 and 2.

†We are indebted to Dr. Fred Lott for this report.



Fig. 1—Liver biopsy section from Case 1. Hematoxylin and eosin, X 100. Chronic hepatitis-cirrhosis, with marked paucity of portal biliary radicles.

Case 2

A 59-year-old white female was found on a routine office visit to have an elevated erythrocyte sedimentation rate and an abnormal BSP retention. The patient denied any physical complaints. Her past medical and family history was noncontributory, except that the patient admitted to five or six cocktails per day. There was no known exposure to hepatitis and no history of transfusions or needle puncture. Physical examination revealed a multilobular thyroid, punctate palmar erythema and palpable, slightly enlarged spleen and liver. The remainder of the examination was essentially normal.

Laboratory data (Table 2) revealed a striking increase of serum alkaline phosphatase, with elevated serum bilirubin, SGOT, increased α_2 and γ globulins, cholesteral and BSP retention. The antimitochondrial antibody and FANA (fluorescent antinuclear antibody) were not significantly increased, nevertheless IgM was at least two and a half times normal. An upper gastrointestinal x-ray showed a pedunculated mass arising from the lesser curvature of the stomach. At operation the gastric tumor was removed, proving to be an inflammatory fibroid of the stomach. An operative cholangiogram and wedge liver biopsy were done. The former was normal and palpation of the common duct revealed no



Fig. 2—Liver biopsy section from Case 2. Hematoxylin and eosin, X 100. Chronic hepatitis, paucity of bile ductules; epithelioid cell granuloma around damaged small bile duct.

TABLE 2
Essential Laboratory Data in Case 2, Female, 59, 1971

Serum	Normal Range	6/22	6/24	6/25	6/26	7/2
Bilirubin (mg%)						
Prompt direct	<0.3	1.9			1.0	1.9
Total	<1.5	3.0			2.1	3.0
Cholesterol, total (mg%)	(150-300)	410	360			333
Triglycerides (mg%)	(30-135)		163			
Alkaline Phosphatase, I.U.	(30-85)	2296	1960			1550
SGOT (units)	(10-50)	166	171			133
Albumin (gm%)	(3.4-4.4)	3.42		3.65		
α_1 globulin (gm%)	(0.1-0.3)	0.27		0.29		
α_2 globulin (gm%)	(0.5-0.7)	1.00		0.80		
β globulin (gm%)	(0.7-1.1)	1.46		1.03		
γ globulin (gm%)	(0.8-1.4)	2.56		2.04		
IgA	(0.14-0.26)			0.2		
IgG	(0.7-1.5)			1.17		
IgM	(0.07-0.13)			0.36		

Additional data: (6/22 to 6/26) Prothrombin time 12.9/12.9; thymol turbidity 12 units; Australia antigen negative; Serum Fe 210, TIBC 338; ESR 70 min/1 hr; antimitochondrial antibody 1:10; serum bile acids: trihydroxy 0.2, dihydroxy 2.6 mg% (normal: 1.4 ± 0.32; 0.43 ± 0.05).

abnormality. Histologic examination of the liver biopsy (Figure 2) revealed a marked infiltrate of chronic inflammatory (round) cells in the periportal spaces. There was a striking paucity of bile ducts and those still present were at times surrounded by epithelioid cells and multinucleated giant cells. There was a very early fibrosis in the portal spaces. No necrosis was seen. These findings were considered to be consistent with a cholangiolitic hepatitis-cirrhosis transition, or early "primary biliary" cirrhosis. Despite the excessive intake of alcohol there was no suggestion of alcoholic hepatitis or fatty metamorphosis.

Comment

Both cases were atypical for chronic cholangiolitic hepatitis-cirrhosis transitions. Neither patient had pruritus nor elevated serum bile acid concentrations and neither exhibited obvious jaundice (though with mild serum bilirubin elevations). One patient had hepatosplenomegaly and nodular cirrhosis; the other a slightly enlarged liver and spleen, but marked chronic hepatitis with very early fibrosis. In both cases, however, the serum alkaline phosphatase was greatly increased and the characteristic histologic evidence of cholangiolysis and granulomata was noted.

In Case 1 the common duct contained some 1 mm stones but there was no evidence of biliary obstruction either in the duct itself or in the liver, thus the cirrhosis was not believed to be of the obstructive or cholostatic type, but rather, in view of the histologic changes, of the primary cholangiolitic type. The minute stones in the gallbladder and common duct may have been caused by a change in composition of the bile due to the diffuse disturbance in the intrahepatic bile ducts.

The failure to find hepatitis associated antigen (HAA) in the blood of either case, is not surprising.

While most cases of cholangiolitic cirrhosis run true to form, there are deviant cases, very difficult to classify.[1,4,21] Granulomas are often encountered in cholangiolitic in contrast with other forms of cirrhosis.[13] It has been suggested that they may represent a reaction to damaged bile duct epithelium or may result from an altered immunologic state. Immunoglobulins, especially IgM and complement have been found by Paronetto and Popper[22] in the bile ducts. Large pyroninophilic cells in the portal tracts around small bile ducts have been shown to contain IgM.[22] Serum antibodies to mitochondria,[10] positive fluorescent antinuclear antibody[10,11] and rheumatoid factor[11] are commonly observed, as well as antibodies to bile duct epithelium[23] and smooth muscle.[10] Increased complement fixation titers have been reported.[6]

Etiology

Drugs

The histologic picture of "primary biliary" cirrhosis, including cholangiolysis, has been observed occasionally in patients receiving tolbutamide,[24] methyltestosterone,[25] and chlorpromazine.[26] Although the histologic change may revert to normal after cessation of the drug, irreversible and even fatal cases of cirrhosis presumed to be on such a chemical basis, have been reported. It may be that such chemicals serve to trigger an abnormal immune response, or chemical allergy, or that they activate a resident virus.

Virus

Recently, Krohn and associates[27] have revived interest in a viral etiology. By electron microscopy, they demonstrated particles similar to the Australia antigen in 11 of 12 patients with "primary biliary" cirrhosis. Antigen and/or antibody were found in nine of ten by means of immunoelectrophoresis. This finding has not yet been confirmed. Kaplan and Grady,[28] using conventional techniques, without electron microscopy, failed to demonstrate the Au antigen in a series of such cases. If the disease is secondary to a virus the usual absence of any history of infectious hepatitis[1,29] will have to be reconciled, possibly on the basis of a peculiar immunologic status.

The renewed interest in a viral etiology calls to mind a remarkable case reported in 1946.[17] The patient had infectious (epidemic) hepatitis at age 15, at which time her sister also had the disease but recovered completely. Thenceforth she had recurrent or waxing and waning jaundice for the remainder of her life. In brief she had long-standing pruritus, chronic jaundice and hepatosplenomegaly. The first biopsy at age 38 revealed chronic hepatitis. Ten years later she had definite cirrhosis on biopsy, which (on recent re-examination*) revealed a marked paucity of small bile ducts in the portal space quite compatible with a "cholangiolitic" hepatitis-cirrhosis transition. One year after this she died from a bleeding esophageal varix. The liver weighed 3,000 gms and presented a somewhat coarsely nodular appearance. It is reasonable to believe

*We are indebted to Dr. Robert Hebbel for examining this with us.

that this was related to the early attack of infectious hepatitis which resulted in a chronic active hepatitis, eventuating in cholangiolitic cirrhosis.

Treatment

No specific therapy is known. The prognosis is uniformly poor although the course is often long and chronic, ranging up to 18 years.[4,29] Treatment with steroids and 6-mercaptopurine has been of little value in halting the progression of the disease. Pruritus has often been satisfactorily controlled with bile acid sequestering resins,[30] although continued use may result in vitamin K or D deficiency, thus promoting a hemorrhagic tendency as well as the skeletal demineralization which the disease regularly imposes in varying degree.

Fischer and Schmid[31] have reported improvement in two cases following treatment with azathioprine. Alarcon-Segovia et al.[32] advocated using azathioprine to alleviate pruritus.

Summary

"Cholangiolitic" or "primary biliary" cirrhosis is a reasonably well defined clinical, immunologic and histologic entity, but cases with dysharmonious features are at times encountered, two of which are described. The term "cholangiolitic" is preferred because of the characteristic cholangiolysis and chronic hepatitis preceding the cirrhosis. Newer knowledge of the disease is reviewed and the relative importance of chemical, viral, and immunologic factors in etiology is considered. The histologic picture of the liver of a case reported 25 years ago, in which a viral etiology was strongly suspected, on re-examination revealed the presence of cholangiolysis, the importance of which had not been recognized at that time.

An important recent paper by Maddrey and associates[33] relating to 68 cases of primary biliary cirrhosis, reports failure to find HAA more frequently than in the population generally.

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26.-33. See page 631.

Acute Hyperthermia with Anesthesia

JOSEF K. WANG, M.D.*

ACUTE HYPERTHERMIA is a rare but potentially fatal complication of general anesthesia. It has followed all forms of general anesthesia. It affects apparently healthy patients undergoing relatively minor surgical procedures. In affected individuals general anesthesia causes a rapid rise in body temperature which, unless rapidly corrected by immediate cooling, is followed by convulsions and death.

The etiology of the acute hyperthermia is unknown, although it has been proposed as an uncoupling of oxidative phosphorylation[1] and as a result of sustained muscular contractions.[2]

A number of families have been reported in whom several members have suffered acute hyperthermia. The tendency to develop this complication appears to be inherited as an autosomal dominant characteristic.[3]

Recent clinical observations strongly suggest a link between this complication and some type of myopathy.[4,5,6,7] Biochemical estimations in the fatal cases showed very high serum-levels of creatine phosphokinase, phosphate and potassium.[4,6] It has also been described in a patient with myotonia congenita.[8]

All patients who are to undergo general anesthesia should be asked about any family history of acute hyperthermia or anesthetic deaths. Suspected patients should be examined clinically and screened by serum creatine phosphokinase levels, so that affected individuals can be warned not to have general anesthetics.[4] Several patients who have survived acute hyperthermia have later had no untoward effect from regional block.[3] Temperature monitoring should be routine during general anesthesia for those suspected so that acute hyperthermia can be corrected at the earliest possible stage.

In almost every instance of reported acute hyperthermia some degree of generalized muscular rigidity preceded the rise in body temperature. Some patients responded to succinylcholine with muscular rigidity. An unusual reaction to succinylcholine, or the development of the generalized muscular rigidity is sufficient grounds for canceling the operation.

Treatment of acute hyperthermia consists of effective cooling and correction of metabolic acidosis. It is not sufficient to apply ice bags to the body surface. Aggressive surface cooling by immersing the patient into ice water bath may be effective in children if begun early. The Wangensteen Gastric Hypothermia Unit affords a quick, simple and effective means of cooling during the period of tremendous heat production.[9] Exchange transfusion with compatible cool blood should be considered. The increased rate of metabolism indicates the necessity of mechanical ventilation with high inspired oxygen concentration. Adequate dosage of sodium bicarbonate or THAM should be given intravenously without hesitation and pharmacological support of a failing circulation is often required. Prophylactic measures, early recognition of this complication and prompt treatment will reduce the high mortality of acute hyperthermia.

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Nasopharyngeal Carcinoma

JUDD H. CHIDLOW, M.D.* AND LAWRENCE W. DeSANTO, M.D.*

In carcinoma of the nasopharyngeal region, the problem is difficult because the site of the lesion is not easily approached and because the lesion is generally diagnosed late and has a tendency to metastasize early. The nasopharynx is hidden by the palatal curtain, is situated under the base of the skull, and is adjacent to the many vital structures in the skull as well as those of the lateral and posterior aspects of the neck.

Fortunately, malignant lesions in this region are relatively rare, comprising 0.05% of all malignancies; malignancies of the head and neck constitute 3%. Orientals, particularly the southern Chinese, have a higher incidence of nasopharyngeal lesions; such lesions account for 0.3 to 0.5% of all cancers. Cancer of the nasopharynx is the most common nasopharyngeal tumor in children and is often misdiagnosed because of the high incidence of malfunctioning eustachian tubes in this age group.

Cause

The cause is unknown, but recent studies have demonstrated high titers of anti-Epstein Barr virus in more than 50% of persons with proved nasopharyngeal cancer. Men are affected three times more often than women and have a poorer prognosis, as is true in most types of malignancies of the head and neck. The average age of the patients is in the fifth decade, and the average duration of symptoms prior to diagnosis is six to nine months. Generally, the patients feel well, until the advanced stage of the disease. The late diagnosis and aggressiveness of most of these tumors and their frequent metastases account for the poor prognosis.

Anatomic and Embryologic Features of the Nasopharynx

The nasopharynx is different embryologically from the lower food and airway passages. Because it develops as part of the nose, morphologically and functionally, the nasopharynx is related to the nose and not to the pharynx; its function is respiratory. This air-containing cavity, which occupies a space 4 by 4 by 2 cm, communicates anteriorly with the nose, laterally with the middle ears, and inferiorly with the oropharynx. The posterior wall is covered by squamous epithelium. The roof and lateral walls back to the eustachian tube orifices are typically covered with stratified ciliated columnar epithelium with mixed serous and mucus secreting glands. In the lateral walls between the patches of squamous and ciliated surfaces, some have found a transitional type of epithelium. The floor, that is, the dorsal surface of the soft palate, is continuous with the nasal passages and is lined with columnar ciliated epithelium. After trauma, whether by the adenotome or by chronic irritation of infection, respiratory epithelium changes to squamous epithelium.

The entire region is transversed by lymphatic vessels. Because these vessels communicate freely across the midline, bilateral metastatic involvement of cervical glands is common. However, one side is usually affected first. From the adjacent retropharyngeal nodes, the upper deep jugular nodes are next involved by tumor spread.

Diagnosis

As with all malignancies, early diagnosis is the key to successful treatment. The inaccessibility of the nasopharynx and the insidious onset of the tumors make early diagnosis particularly difficult. The patient's history and the use of the nasopharyngeal mirror, anterior rhinoscope, and the nasopharyngoscope are helpful in this regard.

Perhaps the earliest symptoms are those of a postnasal irritation, with repeated attempts to clear the throat in an effort to remove the focus of irritation. Usually, superficial ulcers streaked with fresh blood mixed with secretions are apparent next. Ciliary function is altered, leading to stagnation of secretions and halitosis. Nasopharyn-

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geal tumors are not generally rapid growing.

The symptoms and signs are related to direct invasion of adjacent structures and to metastasis (Table 1). For diagnostic purposes, it is useful to categorize the manifestations into four groups: (1) nasopharyngeal, (2) otologic, (3) ophthalmoneurologic, and (4) metastatic. Nasopharyngeal manifestations include obstruction (either unilateral or bilateral), changes in speech (hyponasality or rhinolalia clausa), and anterior or posterior rhinorrhea, usually with bleeding. Otologic symptoms consist of obstruction of the eustachian tube, with conductive hearing loss. There may be otitis media, which is usually serous rather than purulent. All patients with unilateral serous otitis media must have an adequate nasopharyngeal examination. Extension of the tumor from the nasopharynx leads to neurologic abnormalities. All the cranial nerves are vulnerable, but the sixth nerve is most commonly involved. The resulting paralysis of the lateral rectus muscle leads to diplopia. Next most frequently involved, in order of decreasing frequency, are the fifth, third, and fourth cranial nerves. Headaches, difficulty in swallowing, and hoarseness may result if the tumor encompasses the vagus nerve. Metastatic extension, first to the retropharyngeal nodes and then to the upper deep jugular nodes, typically occurs early; a node between the mastoid process and angle of mandible is one of the first to be involved.

TABLE 1
Major Signs and Symptoms of Nasopharyngeal Carcinoma

Sign or symptom	Approximate per cent
Enlarged cervical lymph node	60
Blockage of ear(s)	40
Bloody nasal discharge	30
Nasal obstruction	<30
Speech changes	<30
Double vision	<30

Mirror

A complete ear, nose, throat, and neck examination should be done, after which attention is focused on the nasopharynx. The region is anesthetized with a topical spray. For best visualization, the largest nasopharyngeal mirror possible should be used; a No. 2 mirror usually is adequate. The nose should be constricted with neosynephrine or cocaine and epinephrine for the anterior rhinoscopy examination, and, if necessary, the nasopharyngoscope may be employed. Any bleeding on palpation of the lesion is suggestive of malignancy. Catheters inserted through the nose and out the mouth to elevate the soft palate are useful. Findings may be minimal, such as a fullness in the postnasopharyngeal wall, a narrow fossa of Rosenmüller with intact mucosa, or a compressed torus tubarius. The lateral bands may be enlarged. If there is a nontender node in the upper deep jugular chain, a biopsy specimen should be removed from any suspicious area in the nasopharynx. Submucosal tissue must be obtained, and often several specimens are needed from different areas of the tumors. The tissue should not be squeezed or traumatized any more than is absolutely necessary because this interferes with the microscopic diagnosis, which is difficult even under the best conditions. Roentgenograms of this region are valuable. Findings on sinus films, on roentgenograms of the lateral submento-vertical and occipitosubmental regions, and on tomograms may range from a small mass in the nasopharynx to slight enlargement of the foramina of the skull base or gross destruction of adjacent structures.

The clinical stages of nasopharyngeal carcinoma according to the American Joint Committee[1] in May 1965 are presented in Table 2.

TABLE 2
Clinical Stages of Nasopharyngeal Carcinoma, as Modified From the American Joint Committee[1] Report of May 1965

Stage	Comment
I	Tumor in one site of nasopharynx; that is, I: tumor in posterosuperior wall (valut) and II tumor in lateral wall
II	Tumor in two sites of nasopharynx
III	Clinically palpable cervical nodes that are no fixed
IV	Fixed nodes or distant metastasis

Generally, nasopharyngeal tumors are highly malignant and undifferentiated. The degree of anaplasia in different parts of the same tumor may vary widely from the primary site to the metastatic sites. The site of predilection is probably the fossa of Rosenmüller, but because the tumors usually are large when diagnosed, this is only speculation.

Treatment

Prior to 1900, cancer of the nasopharynx was treated with surgery and electrocoagulation, but the results were unsuccessful. Since that time surgery has had a minor role, being reserved for slow-growing low-grade tumors that rarely metastasize, such as angiofibrosarcomas, malignant

nixed tumors, and cylindromas, all of which are extremely rare in the nasopharynx.

^{60}Cobalt Irradiation

External megavoltage irradiation with ^{60}CO is the chief modality for the treatment of nasopharyngeal carcinoma. This consists of between 6,000 and 8,000 rads to the primary lesion during a six-week period. At the same time a slightly smaller dose is given to the neck, regardless of whether nodes are involved or not. Being thinner than the head, the neck requires about 10% less irradiation. The orbit, paranasal sinuses, and base of the skull are included with the primary site but the doses to each are different, depending on the extent of involvement. The submaxillary and submental nodes are not routinely included because they are rarely sites of metastasis. All other areas in the side of the neck above the clavicles are included, inasmuch as microscopic nests of tumor cells are more readily controlled than are large tumor masses.

Generally, lymphosarcomas are the most radiosensitive and require a lower dose. The more anaplastic the tumor, the better its initial response. Recurrences are frequent. Squamous cell carcinomas give the poorest irradiation response. Tumors that invade bone and nerves are more radioresistant. The shrinkage from treatment reduces pressures on nerves and therefore relieves pain and obstruction. The regression rate of a neoplasm is considered in determining the final dose. Radium seeding or onlays are used only after maximal external irradiation has been delivered.

Supportive therapy during irradiation consists of a high caloric and vitamin diet, dental hygiene, periodic hematologic checks, and careful observation.

The side effects and complications of irradiation thearapy are numerous (Table 3).

Chemotherapy

All cytotoxic drugs have deleterious side effects. The rationale for the prolonged administration of drugs is the subjection of the tumor cells to the continuous action of cytotoxic drugs at various phases of their vulnerability. Antimetabolites and alkylating agents are used most commonly. Evidence indicates that cancer cells are in the systemic circulation early in the disease. Some authors recommend the oral administration of methotrexate, 2.5 mg twice daily for seven to 10 days, to all patients who are being prepared for radiotherapy. However, most authors reserve chemotherapy for palliation after irradiation fails.

Surgery

Radical neck dissection is indicated for uncontrolled neck disease when the primary tumor in the nasopharynx is successfully treated. Occasionally, when neck dissections are done for persistent nodes after irradiation, no viable tumor cells are found.

TABLE 3
Complication of Irradiation in Carcinoma of the Nasopharynx

Site or type	Complication
Mouth	Loss of taste, dryness, mucositis, trismus, dehydration, dysphagia, and anorexia
Teeth	Ischemic devitalization, leading to radionecrosis of those in field (3rd molars especially)
Nasal cavity and paranasal sinuses	Mucositis, ulcers, suppurative maxillary sinusitis, possible fibrous adhesions, and fibrous atresia of choanae
Skin	Erythema, desquamation, blistering, and crusting (with conventional equipment); dry desquamation (with ^{60}Co)
Hair	Temporary epilation
Radiation sickness	Anorexia, nausea, and vomiting
Hemopoietic system	Depression of leukocytes and platelets
Brain stem	Myelitis and possible transverse myelitis
Larynx	Chronic laryngitis (transient); perichondritis (rare)
Bone	Osteitis of vertebrae and sinus walls
Muscles	Atrophy
Eyes	Conjunctivitis, keratitis (rare), and cataracts (rare)
Ears	Depressed cerumen gland in cartilage canal; fibrous muscular fixation, cochlear, and vestibular depression (rare)

Recurrences

Recurrences are common. Within 18 months, 50% of the patients will have recurrences that are clinically apparent, and recurrences have been noted as long as 10 years after treatment. About 30% of the patients will have recurrence at the primary site. Sixty-six per cent will have distant metastasis within two years and 80% within three years. Some radiotherapists use additional irradiation to recurrences, after careful evaluation of the patient. However, for the best chance of cure, the initial external roentgen therapy to the primary site and neck should be maximal. The management of distant metastasis to the skeletal system, liver, or lymph nodes is only palliative, but usually relieves pain. Radium seeds planted beneath the skin into the tumors are also palliative.

Prognosis (Table 4)

The prognosis is more favorable when the patient is young and is female and when the primary lesion is small. If cervical lymph nodes are involved, the prognosis is unfavorable and is even worse when there is bilateral involvement and the nodes are fixed. The time of recurrence after initial treatment is important. Recurrence after two years is associated with a better prognosis than earlier recurrence, as earlier recurrence denotes a more aggressive tumor.

TABLE 4
Average Five-year Survival in Nasopharyngeal Carcinoma

Lesion	Per cent
Early, without metastasis	50
Late, with cervical nodes involved	30
Far advanced	10

The histologic type is also an important factor in prognosis. The lymphoepithelioma and the transitional cell carcinoma are associated with a better progress than is the squamous cell carcinoma. Lymphosarcomas are rare, but respond well to irradiation. The prognosis is poor when the tumors are unclassified.

Summary

Cancer of the nasopharynx is a serious disease for which present modalities of treatment are far from optimal. Early diagnosis, prior to metastasis, offers the patient a better prognosis. Early diagnosis can be accomplished if every physician maintains a high index of suspicion when a patient has symptoms associated with the nasopharynx, ears, eyes, or nerves of the head and neck. The nasopharynx and neck must be carefully examined. The prognosis is poor for patients with nosopharyngeal carcinomas because of the insidious nature of the tumors and their tendency for early metastasis even before any symptoms are manifest.

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Meeting

Minnesota Society of Anesthesiologists.

Fall Scientific Meeting
Minnesota Society of Anesthesiologists

September 16, 1972—Marriott Motor Inn
Bloomington, Minnesota

"Shock Lung," plus related subjects

Dr. James Wilson, Duke University, Durham, North Carolina.

What's in a word? Consider the difference between wise guy and wise man.

Iodine Metabolism in Thyroid Function

HEINZ W. WAHNER, M.D.*

In analyzing thyroid function one wishes to elucidate two factors: (1) the level of the metabolic function of the body—that is, of hypothyroid, euthyroid, or hyperthyroid; and (2) the nature of the thyroid disease. In both of these approaches we make use of radioactive tracers, since the metabolism of the thyroid hormone is closely related to the metabolism of iodine. An understanding of thyroid function and a reasonable approach to the interpretation of thyroid function tests necessitates a thorough understanding of iodine metabolism.

Isotopes of Iodine

The isotopes of iodine used in thyroid testing and investigation are shown in Table 1. All emit gamma rays of various energies, ranging from 27 to 780 kev, and have half-lives ranging from two hours to 57 days. Some also emit beta particles. Beta particles emitted from isotopes of iodine cannot be used for external counting in-vivo because of their small tissue half-value layer, but they are effective in treating thyroid disease. ^{131}I and ^{125}I are used most frequently for clinical diagnostic and therapeutic purposes.

Regulation of Iodine Metabolism

The regulatory mechanism of iodine metabolism is diagrammed in Figure 1. Thyroid hormone acts on peripheral tissue to set the level of metabolism and is in turn itself degraded. As hormone is used in the peripheral tissue, the blood level decreases. This change is sensed by the pituitary and hypothalamus, TSH secretion is increased, and more thyroid hormone is secreted by the thyroid gland. The tissue action is the prime element in this sequence. The remaining elements serve to provide a constant supply to the tissues. This feedback mechanism regulates important parameters of iodine metabolism and is an important step which can be evaluated by laboratory methods such as the T3 suppression[1] and TSH stimulation tests.[2] TSH also can be measured directly by radioimmunoassay.[3] These three tests allow a differential diagnosis of primary (thyroid) and secondary (pituitary) hypothyroidism.

TABLE 1
Isotopes Useful in the Investigation, Diagnosis, and Treatment of Thyroid Disorders

Isotope	Half-life	Average β Emission (kev)	Equivalent β Emission Xray (kev)	Predominant γ Emission (kev)
^{123}I	13 hr	0	31	160
^{125}I	57 days	0	21	27
^{131}I	8 days	190	Negligible	364
^{132}I	2.3 hr	490	Negligible	670
				780
^{99m}Tc	6 hr	0	14	140

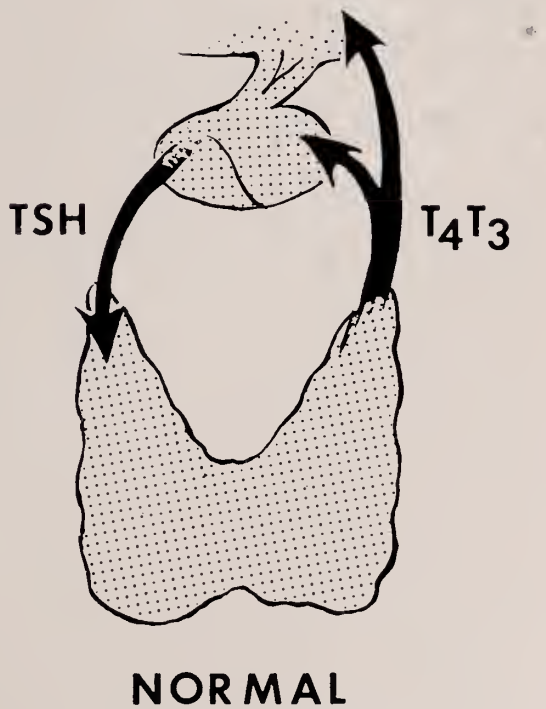


Fig. 1—Normal feedback mechanism which regulates the synthesis and secretion of thyroid hormone. (From Gorman, C. A., and McConahey, W. M.: Diagnosis of Hyperthyroidism and Hypothyroidism by Laboratory Methods. Med. Clin. N. Amer. 54:1037-1047, 1970. By permission of W. B. Saunders Company.)

*Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

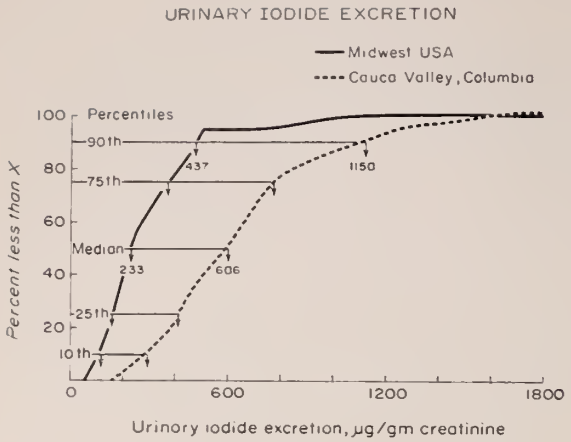


Fig. 2—Urinary iodide excretion in 185 subjects from endemic goiter area of Colombia, South America, and 66 subjects from middle western United States. Note higher urinary iodide excretion in subjects from Colombia.

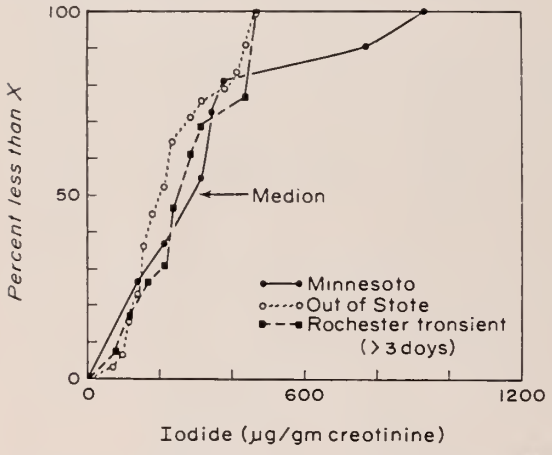


Fig. 3—Iodide excretion in 11 subjects from Minnesota, 42 subjects from other states of United States, and 15 subjects living in Rochester for more than three days. Note that there is very little difference in these groups.

Iodine Intake

Dietary iodine intake may vary from less than 50 µg/day, when we call the diet iodine-deficient, to more than 3,000 µg/day, as seen in the seaweed eaters in some Japanese islands. Other sources of iodine are drugs, food preservatives, skin lotions, and roentgenographic contrast media. The amount of iodine ingested is of paramount importance for the interpretation of all tests using radioactive tracers in—vivo. Therefore, before normal values are defined for a population, the range and the mean of the daily ingestion of iodine should be established. An accepted way to estimate the daily iodine intake is to measure the daily urinary iodine excretion.

The magnitude of the variation in iodine intake which may be expected is shown in Figure 2 which compares a population from Colombia, South America, and one from Rochester, Minnesota. That patients from various parts of the United States have about the same iodine intake is shown in Figure 3. In our affluent society, national food sources and habits are more important than location within a country. Several recent articles have demonstrated that normal ^{131}I uptake values are lower now than 10 years ago. This is because of an increase in dietary intake.

Metabolism of Inorganic Iodide

Ingested iodide is absorbed rapidly through the mucosa of the entire gut. Because of this rapid absorption, no clearcut evidence of iodine deficiency due to malabsorption has ever been documented. The iodide then circulates in the blood

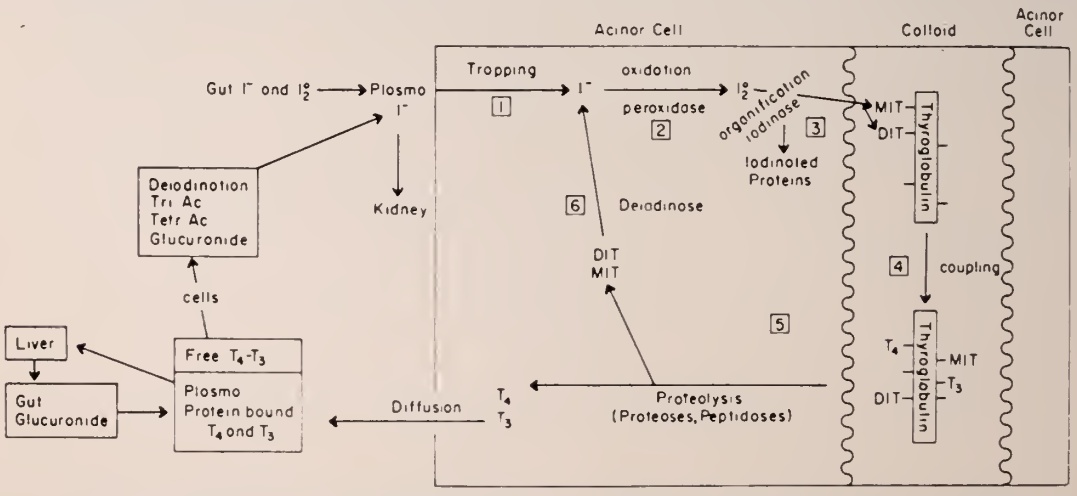


Fig. 4—Schematic representation of iodine metabolism. Arabic numerals depict known steps in hormone synthesis. (From Goodman, R. M.: Genetic Disorders of Man. Boston, Little, Brown & Company, 1970, p. 654. By permission.)

and is actively transported into thyroid tissue which maintains a 20- to 40-fold concentration gradient over the level of plasma (No. 1 in Figure 4). The iodide trap is estimated by early uptake measurements, Berson clearance, and techniques with pertechnetate ^{99m}Tc. Iodide can be discharged from the trap by perchlorate or thiocyanate, which is the basis for the perchlorate discharge test.

Through the action of a peroxidase and peroxide-forming enzymes, iodide is oxidized (No. 2 in Figure 4) and bound to tyrosine in thyroglobulin (No. 3). Organification is blocked by the thiourea drugs and a number of goitrogens. Iodinated tyrosine molecules in thyroglobulin are coupled to form iodothyronines (T3 and T4) (No. 4).

Thyroglobulin is synthesized on ribosomes in the thyroid cell, is transported slowly from the cell into the colloid, and is iodinated at the interface between cell and colloid. Iodinated thyroglobulin is stored in the colloid for an extensive period, averaging 50 to 100 days in healthy man.

For secretion, the colloid undergoes pinocytosis at the apical cell border, and colloid droplets are formed inside the cell. Fusion of lysosomes with these droplets produces a phagosome with a low internal pH, in which proteolytic enzymes and peptidases can degrade thyroglobulin into its component amino acids (No. 5).

The released T3 and T4 are secreted into the blood while the iodotyrosines are deiodinated and their iodide is recircled inside the gland (No. 6). The sequence so far can be evaluated by the thyroid uptake of ^{131}I. Conversion ratio and PB^{131}I are measurements of the speed with which ^{131}I is transformed into and excreted as hormone.

GENERAL OUTLINE

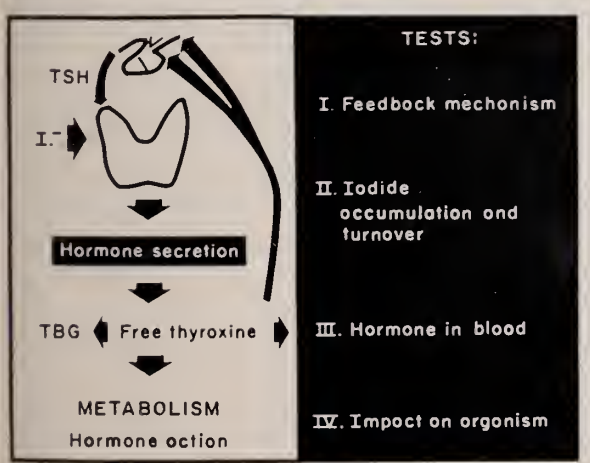


Fig. 5—Relationship of tests to thyroid physiology.

Metabolism of Organic Iodine

Normally, the thyroid gland secretes about 100 μg of thyroxine (T4) and 50μg of triiodothyronine (T3) per day. Alterations in the T4/T3 relationship have only recently been recognized as definable disease entities. The term "T3 hyperthyroidism" has been coined.[4,5] This ratio also may be altered in iodine deficiency,[6] in toxic nodular goiter,[7] as a premonitoring manifestation of thyrotoxicosis,[8] and after treatment with ^{131}I[9]. A correlation between elevated LATS levels and serum T3 levels has been found.[8] When T3 is significantly higher than normal, thyroid function tests may be difficult to interpret. The Sterling method[10] and a radioimmunoassay[11] are now available to measure T3 in serum; the normal value for the Sterling method is 220± 40 (SD) ng/100 ml.[12] About 30% of the total T3 in the blood is derived from conversion of T4 to T3 in the peripheral tissues.

Iodinated albumin is formed in association with iodothyroglobulin and may be released in small amounts normally, but this may be significantly increased in Hashimoto's thyroiditis or in rare patients with thyroid carcinoma. Also, some thyroglobulin is released into the circulation, probably via the lymphatics. Some iodide leaks from the thyroid gland, and iodotyrosines are found in the circulation in the presence of very hyperplastic glands.

In the blood T4 is bound to transporting proteins: thyroxine binding globulin (TBG), 75%; thyroxine binding albumin (TBA), 10 to 15%; and thyroxine binding prealbumin (TBPA), 10%. Approximately 0.05% of thyroid hormone remains free (FT4). An equilibrium exists between the bound and the free hormone. PBI, BEI, and total T4 are measurements of circulating thyroid hormone levels. TBG can be measured electrophoretically or by a simple charcoal adsorption method.[13]

Most modern thyroid laboratory screening tests are based on hormone measurements in the blood. An increase in thyroid binding proteins results in an increase in total circulating T4 but generally not in free T4. Exceptions are recognized. Distinct quantitative abnormalities of TBG, induced or congenital, are recognized and have to be considered in the interpretation of laboratory tests. Here free T4, direct determination of TBG, and T3 uptake tests are of importance.

T4 has a half-life of seven days in the blood. T3 has a half-life of 1.5 days. The disappearance rate of injected labeled hormone can be used as index of the cellular utilization of the hormone for the diagnosis of thyroid disfunction (specific activity test). In the cells thyroid hormone is degraded and the liberated iodine is partly recycled and partly excreted as iodide in the urine. There exists an enterohepatic circulation of conjugated T4, which is excreted in the bile, but this is of minor importance in man, and only in cases of severe gastrointestinal disorders or biliary diversion may it affect some tests.

Information about the size, position, and form of the gland can be obtained from the thyroid scan. The distribution of the tracer within the gland is also of diagnostic importance (cold and hot areas).

Summary

The thyroid lends itself to testing at four levels (Figure 5). The tests we use most frequent are illustrated in Table 2.

Acknowledgment

I acknowledge the help of Dr. C. A. Gorman and Dr. W. M. McConahey in discussions of this subject.

TABLE 2

Levels at Which Thyroid Function May Be Tested

LEVEL	TESTS*
Tests of pituitary thyroid interrelationship	*T3 suppression test* *TSH immunoassay* TSH stimulation
Accumulation of ^{123}I by thyroid and its distribution within gland	*^{131}I uptake* *Thyroid scan*
Concentration of circulating thyroid hormone	PBI and BEI *Total T4* *Free T4* Red cell T3 uptake (indirectly)
Impact of thyroid hormone on body	*BMR* Cholesterol *Reflex relaxation time*

*Italics show tests we use most frequently.

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What creature is in health, either young or old,
But some mirth with modesty will be glad to use . . .
For mirth prolongeth life and causeth health;
*Mirth recreates our spirits and voideth pensiveness.**

*Nicholas Udall: Ralph Roister Doister, prologue, 1566/7.

Intussusception: Revisited

The Duluth Experience from 1921—1966

JOHN V. THOMAS, M.D.

A STUDY OF intussusception in Duluth brought to light not only some interesting facts but uncovered a previous report on this same clinical problem presented by Dr. F. H. Magney. Dr. Magney's paper appeared in *Minnesota Medicine* 25 years ago. His study, plus the current data, provide an opportunity to observe this disease as experienced by the physicians in Duluth from 1921 thru 1966.

Summary of Dr. Magney's Study

In 1947 Dr. Magney described 25 years of experience with those cases subjected to surgery for intussusception. He stated: "The majority of Duluth physicians are of the opinion that the treatment is strictly surgical, and the so-called conservative methods were not attempted." Of 31 cases operated, when simple reduction of the intussusception was the only manipulation, there were eight deaths for a mortality of 28%. Of seven cases where resection and anastomosis and/or enterostomy were done, there were four deaths, 57% mortality. The overall mortality of 58 operations for intussusception was 26% (15 deaths). Dr. Magney called attention to improved measures of pre- and postoperative care by pointing out that whereas the mortality from 1921 to 1931 was 46.7%, the succeeding years from 1931 to 1946 showed only an 18% mortality. He underlined this fact by noting only two deaths among 17 patients operated between 1941 and 1946.

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Present Study

For this report the medical records departments of St. Luke's and St. Mary's Hospitals selected all charts bearing the diagnosis of intussusception for the years 1939 to 1966, inclusive. Only those cases are reported in which a positive diagnosis could be made on the basis of recorded historical and physical findings and radiological or operative confirmation. A total of 86 cases in 84 patients was found. There were eight examples of intussusception in adults. Seventy-eight cases occurred in 76 children, all less than 13 years of age. Five patients died prior to 1951. All were children. The two recurrent cases will be described in detail.

Intussusception in Children

Age incidence in young children is demonstrated in Figure 1. Seven cases occurred from age four to 13 years and are not included in this figure. Seventy-seven percent were less than 24 months of age, and 63% were less than 12 months of age. Annual incidence of intussusception in Duluth between 1939 and 1966 is seen in Figure 2. No

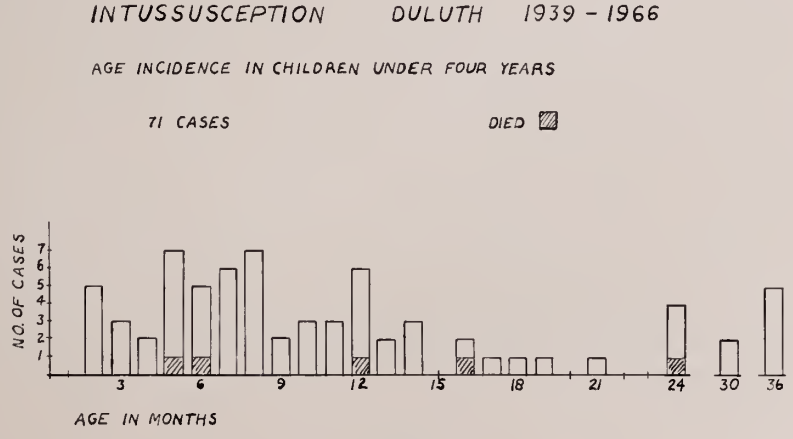


Figure 1

deaths were recorded between 1951 and 1966. Forty-three of the 76 children were male; 33 were female.

Intussusception is usually a sudden, abrupt incident in the life of an otherwise healthy child. Of the 78 examples, 61% exhibited symptoms for less than 24 hours prior to examination, and of these, more than half were examined within 12 hours of the onset of symptoms. Only 13% were first examined between 24 and 48 hours after onset of symptoms, and 23% after more than 48 hours of symptoms.

Dr. Magney emphasized that the three cardinal signs and symptoms of this disorder are intermittent colicky pain, vomiting, and bloody stools. In his report, 75% of 58 children showed all three and all of the cases exhibited at least one of these three symptoms.

In the present series, 65% of children have a history of bloody stool, passed a bloody stool when examined, or showed blood on the examiner's rectal glove. Vomiting occurred in 56%; abdominal cramps in 54%. An abdominal mass palpable in 41%, but in only 22% was the leucocyte count more than 15,000, and only 10% showed abdominal distension.

Treatment of Intussusception in Children

The paper by Dr. Magney, covering the period 1921 through 1945, reports only patients treated surgically. His statement that "the treatment is strictly surgical" reflects the prevailing concept of therapy during this period. Ware and Coffey[7] in 1950 were of the opinion that x-ray studies consumed time to the detriment of the child's welfare and that treatment was always early surgery.

For the present review of intussusception in Duluth, the mode of treatment was used to divide the patients into three groups: those treated by barium enema reduction alone; those treated by operative intervention alone; and those treated by barium enema followed by surgery because of failure of reduction. See Figure 3.

Group A, those treated by barium enema alone, (28 cases). In three patients the barium enema was negative and the charts suggested "spontaneous" reduction or reduction without radiographic demonstration. In 25 cases, hydrostatic reduction was accomplished; in 13 instances from the right colon, six times from the transverse colon, only twice from the left colon, and unspecified in four cases. There were no deaths and no complications recorded in this group.

Group B, those treated by surgery alone, (30 cases). Manual reduction as the only necessary surgical manuever was successful in 22 patients and no obvious mechanical cause for the intussusception was described. Ileo-ileal intussusception occurred only one and in this case two separate sites were reduced. Resectional surgery was necessary in the remaining eight cases. In one patient a necrotic Meckel's diverticulum leading the intussusception was excised, but in two cases where a Meckel's diverticulum was the leading point, it was necessary to include a segment of ileum in the resection. In one patient an ileal segment containing a benign polyp was

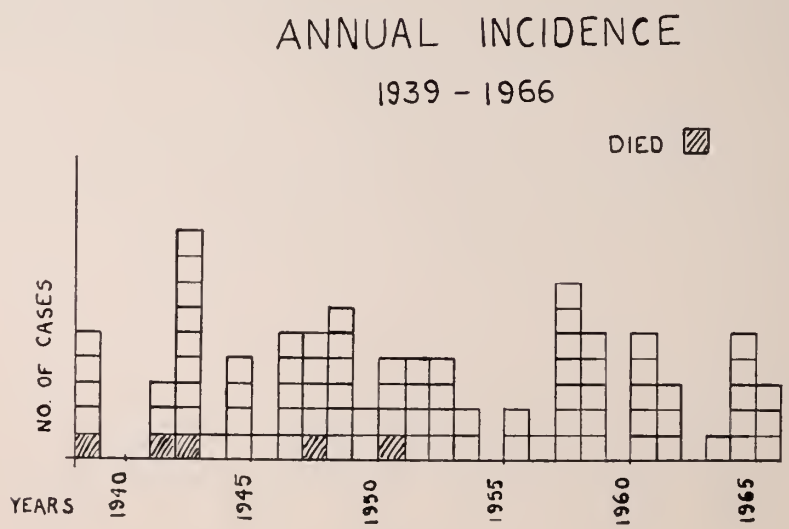


Figure 2

excised. Resection of a necrotic ileal segment was necessary once, right colectomy once, and resection of an ileo-colic segment twice. Appendectomy was performed seven times and the appendix was found to be acutely inflammed in three of these instances. Cecostomy was done in one patient and in five patients suture fixation of the terminal ileum was an additional procedure.

Group C, those treated by barium enema followed by surgical exploration, (20 cases). In two patients, the barium study was negative but the patients were explored, ileo-ileal intussusception found and manually reduced. In four instances, after positive x-ray evidence of obstruction, exploration failed to disclose an intussusception. Manual reduction at operation was successful in 11 cases. In one patient a Meckel's diverticulum was found to be the leading point and was excised. A Meckel's diverticulum, not thought to be causal, was excised from another patient. Segmental ileal resection was necessary twice, and excision of an ileo-colic segment once. In a single case, operative reduction was successful and a Meckel's diverticulum was noted, but excision was deferred and the diverticulum and the appendix were removed at a second operation one month later. Appendectomy was done in six cases; the appendix showed acute inflammation twice. Enterostomy was employed only once.

Complications and Mortality

The table lists all complications which occurred in Groups B and C. Of the 76 children treated for intussusception between 1939 and 1966, there were five deaths, a mortality rate of 6.6%. The five deaths occurred during the first 12 years of this study, among the first 45 cases collected. There were no recorded deaths related to intussusception between 1951 and 1966.

Case Reports

Case 1, 1939

A boy, aged five months, having had diarrhea for three days, bloody for one day, with vomiting, was admitted with a hemoglobin of 9.2 gm %. A barium enema done 24 hours after admission revealed an obstructing mass in the descending colon. At operation, an ileo-colic intussusception was reduced from the descending colon, and the bowel was observed to become pink. Postoperatively fever rose to 105° and the child expired 72 hours later. Autopsy revealed a necrotic right colon with perforation and peritonitis.

Case 2. 1942.

A two-year-old boy, with congential absence of the legs and right hand, was admitted with a five hour history of abdominal cramps, diarrhea and bloody stool. A rectal mass was palpable. Taken to surgery, anesthetic problems were encountered. An ileo-sigmoid intussusception was manually reduced but the child expired a few hours later due to vomiting and aspiration.

Case 3. 1943

A one-year-old female, with mongolism, was ill for 24 hours with abdominal pain and bloody stool, and an abdominal mass was palpable. A barium enema demonstrated an irreducible ileocecal intussusception. At operation successful reduction and excision of a Meckel's diverticulum was accomplished. The child expired five hours later. Autopsy revealed an interventricular septal defect.

Case 4. 1948

A girl, aged six months, had been ill for two days with

TABLE
Complication of Surgical Treatment of Intussusception in Children

	Surgery 30 Cases	B.E. + Surgery 20 Cases
Wound Infection	2	
P.O. Ileus	2	
Dehiscence		1
Fistula		1
"Stormy" Recovery	1	
Death	2	3

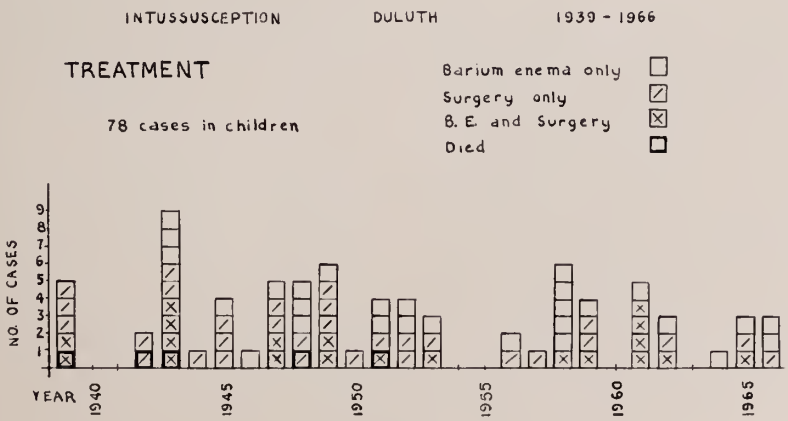


Figure 3

vomiting and bloody diarrhea. Dehydration was marked and a rectal mass palpable. Temperature on admission was 102° and the white count 16,800. She was given parenteral fluids but continued to vomit and have bloody diarrhea. Moribund, she was explored 26 hours after admission. An intussusception was reduced from the sigmoid and a necrotic cecum found. A right colectomy was done but the child expired in surgery.

Case 5. 1951

A girl, 16-months-old, vomited for three days, then had a bloody stool and was admitted. A mass was palpable in the left lower quadrant. A barium enema failed to completely reduce the intussusception. At operation, reduction was completed but gangrene of the terminal ileum required a segmental ileal resection. Postoperatively she was toxic with fever and vomiting. Gastric suction was employed but she expired 72 hours later. Autopsy revealed peritonitis due to anastomatic disruption and also pulmonary atelectasis.

Recurrent Intussusception

Two children exhibited recurrent episodes of intussusception, an incidence of 2.6%.

Case 6

A seven-month-old female, admitted with pain, vomiting and an abdominal mass, produced a bloody stool after an enema. An ileo-colic intussusception was reduced at operation. One month later she was admitted because of a bloody stool and an abdominal mass was again palpable. A barium enema failed to completely reduce the intussusception; operative reduction was successful. At surgery an acutely inflammed appendix was removed.

Case 7

A three-month-old girl was admitted after two hours of abdominal pain and passed bloody mucus from the rectum. A barium enema demonstrated but incompletely reduced an intussusception in the mid-transverse colon. Manual reduction of an ileo-colic intussusception and appendectomy were performed. Three years later, during a bout of upper respiratory infection, she complained of abdominal pain and nausea for 24 hours. No mass was palpable, but barium enema at this time successfully reduced an intussusception from the transverse colon.

Intussusception in Adults

Eight cases were found involving adults from ages 33 to 80 years; five were male. None passed blood by rectum. Pain and vomiting were predominant symptoms. In two cases a mass was palpable. A barium study of the colon was done in only two cases and demonstrated an ileal polyp in one, and a mass in the transverse colon of the other. All but one were surgically explored; the exception was a terminal patient with extensive metastases of melanocarcinoma. Manual reduction of the intussusception was performed in three patients, removing an intramural lipoma from two and the appendix from the third. A segmental ileal resection was necessary in three patients: an intramural lipoma, a fibroma, and a Meckel's diverticulum leading the intussusception in these cases. In one patient a carcinoma of the cecum was the point of the intussusception and necessitated a right colectomy.

Discussion

Although the etiology of intussusception has produced a great deal of speculation, most of the interest in this disease has focused upon treatment. Surgery continues to be the primary approach. Abbott, Cabell and Creech[1] in 1962 reported 96 cases in children, having used hydrostatic reduction in only 13 cases, with successful reduction in ten. Benson, Lloyd and Fischer[2] reported 300 cases in 1963, employing hydrostatic reduction only 25 times. Swenson and Oeconomopoulos[6] in 1962 reported 97 cases in children, using barium enema reduction only eighteen times but adding that the barium study was used diagnostically in twenty additional cases. These latter authors describe the advocates of reduction by barium enema as overenthusiastic. Among their criticisms of the hydrostatic method they included the uncertainty of satisfactory reduction, possible rupture of necrotic bowel, the loss of valuable time, and the fact that ileo-ileal intussusception cannot be reduced.

The 1959 monograph by Ravitch[4] describes in detail the use of hydrostatic reduction of intussusception and reports that 69% of 77 cases were successfully treated by this method without mortality. Dr. Ravitch emphasizes that barium enema reduction is applicable to all cases but that it must be a surgically supervised procedure, simultaneous with gastric lavage, blood and fluid replacement when indicated. The operating room should be in preparation while the barium enema is being administered, and at the first indication of incomplete or unsuccessful reduction laparotomy should be immediately undertaken.

The series here reported indicates that barium enema reduction was employed in 48 of the 78 cases in children, with successful reduction in 28 cases: a 58% success rate. It is also of interest to observe that among the first half of the study, those 39 cases from 1939 through 1950, a barium enema was used 20 times with successful reduction in 10 cases. In the second half of the study a barium enema was attempted 28 times with 18 successful reductions. Surgery was the primary approach in 19 cases of the first half but in only 11 instances from the latter portion of this study.

Recurrent intussusception was observed in two patients, both under one year of age. Soper and Brown[5] reviewed the literature collecting over

5000 cases, including 184 recurrences or 3.35%. However they reported that hydrostatic reduction was followed by a 9.96% recurrence rate, surgical reduction by only 3.1% recurrence. These authors noted that children exhibiting recurrent intussusception are more likely to demonstrate a specific etiologic mechanism, especially those children over eight years of age. They recommend that a second recurrence of intussusception be treated surgically and the involved intestine resected if the intussusception is the same type as had previously occurred.

Summary

This report provides an interesting review of the incidence and treatment of intussusception as observed and altered by the professional community of Duluth from 1921 through 1966. Two major trends are obvious: one, the abrupt change in mortality of this disease which accompanied the gains made in anesthesia, surgical technique, diagnostic methods and pre- and postoperative care; and second, the transition in approach to treatment from that exclusively surgical to a choice of method dependent on clinical features and diagnostic procedures. The low morbidity of barium enema reduction is noteworthy.

With regard to the etiology of intussusception, the reported cases illustrate the infrequency with which the surgeon can demonstrate a mechanical factor in children, and the converse observation in the adult when almost all cases showed a tumor leading the intussusception.

Intussusception does recur and should be considered as an entirely new event, with treatment based on the same tenets, with awareness however that a mechanical factor will be found more frequently in the older child.

Deaths from delay in treatment should not occur. Intussusception presents the physician with a unique example of bowel obstruction, usually in an infant, by nature ill-equipped to withstand abrupt changes in fluid and electrolyte balances. Treatment should be based on careful examination and a cautious trial of radiologically controlled hydrostatic reduction. Supportive measures include fluid and blood replacement when indicated. Prompt surgical intervention is dictated by signs of intestinal perforation or failure of hydrostatic reduction.

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*Every man desires to live long, but no man would be old.**

*Jonathan Swift's essay: Thoughts on Various Subjects.

Laboratory Letter

Screening for Something That Makes A Difference

"Aim high. Aim for something that makes a difference."—Peter F. Drucker

EACH YEAR 600,000 Americans die from coronary artery disease or its consequences. 165,000 of them are under 65.

One of the ways to cut this coronary count is to spot the man who's coronary prone.

Measuring Cholesterol and Triglycerides

How? We know of no better way than measuring a man's cholesterol and triglyceride levels, then, if either is elevated, determining his type of hyperlipoproteinemia.

Levels in Men with Infarcts

Consider this evidence. If you take a group of "normal" men in their fifties and measure their cholesterol and triglycerides, about 25 percent will have an elevated value of one or another test.[1] But take a group under 55 who have had myocardial infarcts, and the incidence of abnormal lipids jumps to nearly 60 percent.

Higher the Levels, Greater the Risks

Or look at it this way. Men who have cholesterol or triglyceride levels in the upper "quintile" (upper 20 percent of lipid levels in the population) run five to seven times the risk of myocardial infarction as those in the lower quintile.[2]

Phenotypes

Now, a little on hyperlipoproteinemia phenotypes: I, II, III, IV, and V. For practical purposes type I (a rare familial disease occurring mostly in children) and type V (a heterogeneous disorder characterized by abdominal crises and often secondary to other disease) have nothing to do with myocardial infarctions or coronary artery disease.

Types II, III, and IV

This leaves types II, III, and IV. Of these, type II and IV account for most people suffering from coronary artery disease. Type III is less common and usually manifests itself as peripheral arteriosclerosis. Other than these clinical differences, the main reason for separating hyperlipoproteinemias into types is that each type responds to different diets and drugs.

Preventing Infarcts

If we're going to prevent myocardial infarcts, we'll have to identify who's susceptible early enough. At present, the best way to do that is to measure serum cholesterol and triglycerides.

Knowing these levels could make a difference.

Any pathologist wishing to contribute material for this section is invited to do so.

Richard L. Reece, M.D.
Minneapolis, Minnesota

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Indications: For the treatment of trichomoniasis in both male and female patients and the sexual partners of patients with a recurrence of the infection provided trichomonads have been demonstrated by wet smear or culture. The oral form is indicated also for intestinal amebiasis and amebic liver abscess.

Contraindications: Evidence or history of blood dyscrasia, active organic disease of the CNS, the first trimester of pregnancy and a history of hypersensitivity to metronidazole.

Warnings: Use with discretion during the second and third trimesters of pregnancy and restrict to those pregnant patients not cured by topical measures. Flagyl (metronidazole) is secreted in the breast milk of nursing mothers. It is not known whether this can be injurious to the newborn.

Precautions: Mild leukopenia has been reported during Flagyl use; total and differential leukocyte counts are recommended before and after treatment with the drug, especially if a second course is necessary. Avoid alcoholic beverages during Flagyl therapy because abdominal cramps, vomiting and flushing may occur. Discontinue Flagyl promptly if abnormal neurologic signs occur. Exacerbation of moniliasis may occur. In amebic liver abscess, aspirate pus during metronidazole therapy.

Adverse Reactions: Nausea, headache, anorexia, vomiting, diarrhea, epigastric distress, abdominal cramping, constipation, a metallic, sharp and unpleasant taste, furry or sore tongue, glossitis and stomatitis possibly associated with a sudden overgrowth of *Monilia*, exacerbation of vaginal moniliasis, an occasional reversible moderate leukopenia, dizziness, vertigo, incoordination and ataxia, numbness or paresthesia of an extremity, fleeting joint pains, confusion, irritability, depression, insomnia, mild erythematous eruptions, "weakness," urticaria, flushing, dryness of the mouth, vagina or vulva, pruritus, dysuria, cystitis, a sense of pelvic pressure, dyspareunia, fever, polyuria, incontinence, decrease of libido, nasal congestion, proctitis, pyuria and darkened urine have occurred in patients receiving the drug. Patients receiving Flagyl may experience abdominal distress, nausea, vomiting or headache if alcoholic beverages are consumed. The taste of alcoholic beverages may also be modified. Flattening of the T wave may be seen in EKG tracings.

Dosage and Administration

For Trichomoniasis. In the Female: One 250-mg. tablet orally three times daily for ten days. Courses may be repeated if required in especially stubborn cases; in such patients an interval of four to six weeks between courses and total and differential leukocyte counts before, during, and after treatment are recommended. Vaginal inserts of 500 mg. are available for use, particularly in stubborn cases. *When the vaginal inserts are used,* one 500-mg. insert is placed high in the vaginal vault each day for ten days and the oral dosage is reduced to two 250-mg. tablets daily during the ten-day course of treatment. Do not use the vaginal inserts as the sole form of therapy. *In the Male:* Prescribe Flagyl only when trichomonads are demonstrated in the urogenital tract, one 250-mg. tablet two times daily for ten days. Flagyl should be taken by both partners over the same ten-day period when it is prescribed for the male in conjunction with the treatment of his female partner.

For Amebiasis. Adults: For acute intestinal amebiasis, 750 mg. orally three times daily for 5 to 10 days. For amebic liver abscess, 500 to 750 mg. orally three times daily for 5 to 10 days.

Children: 35 to 50 mg./kg. of body weight/24 hours, divided into three doses, orally for ten days.

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Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

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Editorials

1922: A Vintage Year for Minnesota Medicine

A DISTINGUISHED group of physicians began their practice in Minnesota in 1922 and now are being honored by induction into the Fifty Year Club of the Minnesota State Medical Association.

At the time of their graduation, most of them from the University of Minnesota Medical school, Warren G. Harding was the president soon to be replaced by his vice president, Calvin Coolidge. Jacob Preuss was Governor of Minnesota and J. F. Corbett, president of the MSMA. On the local scene in 1922 Lawrence Hodgson was mayor of St. Paul and across the river the mayor was General George E. Leach.

At the Palace Theater was playing "Adventures of Tarzan" with Elmo Lincoln, a serial with 15 electrifying episodes.

Thumbing through the *Saturday Evening Post* for 1922 one finds advertisements for versatile kitchen stoves that would burn coal, wood, *and* gas. One could buy marvelous cars with names like Jordan, Kissel, and Maxwell that certainly were beyond the reach of the medical class of '22. The affluent could buy a Chevrolet or Ford Roadster for about $500, but the majority transported their dates about town on the yellow street-cars that took them anywhere for five cents. However in the newspapers were letters to the editor complaining of the imminent raise of fare to six cents.

The Minneapolis Journal reported, "Minneapolis Symphony Orchestra, Emil Oberhoffer, conductor, soloist Engelbert Roentgen, violoncellist, perform a concert at 3:30 in the Minneapolis Auditorium."



1922 Ford Model T Roadster—Preferred transportation for medical students in 1922.



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Should children be deprived of milk because of "lactose intolerance?"

No, according to the Protein Advisory Group of the United Nations.

In a special report, the PAG stated, "It would be highly inappropriate, on the basis of present evidence, to discourage programs to improve milk supplies and increase milk consumption among children because of fear of milk intolerance." The statement emphasizes that low lactase activity and results obtained in tests with high lactose loads are not adequate indications of milk intolerance.

The statement also affirms the advisability of using milk as an excellent source of protein in child feeding programs.

Dairy Council is sponsoring further research on lactose intolerance. This is just another of the many areas of interest of Dairy Council, in the pursuit of better health for everyone through sound nutrition practices.

Dairy Council of the Twin Cities, St. Paul, Minnesota
A primary resource for nutrition education.
Affiliated Unit of National Dairy Council

About this time 50 years ago A. E. Benjamin presided at a meeting of the Hennepin County Medical Society in the medical library of the Donaldson Building, and Dean E. P. Lyon addressed the group on the subject: The medical school and public welfare. He said: "Last year we had 200 applicants, but only 103 of these were wholly free of scholarship deficiencies. Of the 103 we accepted, 86 . . . The medical school looks forward to such an increase in its facilities as will permit the enrollment of all students who desire to secure their medical education at the University of Minnesota."

Dean Lyons' address was printed in Volume 42 of *The Journal-Lancet*. From that reference and from Volume 5 of MINNESOTA MEDICINE are culled the following:

"It was said in a recent issue of the *Daily Press* of Minneapolis that the doctor's whiskey-pad saves 98,782 victims of colds in the year."

"Dr. W. J. Mayo delivered the John B. Murphy address before the American College of Surgeons in Philadelphia at which meeting honorary fellowship was conferred upon him and Dr. C. H. Mayo."

"Dr. Thomas J. Kinsella (Minnesota 1919), and Dr. Edward A. Regnier (Minnesota 1921) have become members of the Nicollet Clinic, Minneapolis, in the division of surgery."

"Physicians in Duluth are constantly asked if it is not advisable for patients with chronic throat and lung afflictions to seek a milder and presumably better climate than Duluth. There is quite a general impression among those not well informed on the subject that there are undesirable features about the climate of Duluth . . . As a matter of fact the climate of Duluth and vicinity is in many respects very similar to that of the Adirondack Mountains in the State of New York, known the country over as a popular resort, summer and winter, for patients suffering from pulmonary and throat diseases." [Note the careful avoidance of the word tuberculosis.]

Advertisement: "The Curtis Northwest Airplant Company has opened an office at the Curtis Hotel in Minneapolis and offers emergency service to members of the profession."

Advertisement: "Lewisville, Watonwan County, a town on the Omaha road midway between Madelia and Fairmont with a population of 229 (1920 census) is in need of a resident physician. Communications should be addressed to the mayor."

"During the last few years such important physical and technical advances have been made with the aid of *x-rays* that it might not be far from correct to class the discovery of Professor Roentgen as one of the most important of the last quarter of a century."

Book Review: The Place of Version in Obstetrics. Irving W. Potter. Mosby $5.00. . . . "Let no one lose sight of the fact that Dr. Potter is a mighty clever obstetrician and that on the whole he is getting comparatively good results with his methods of delivery. His first paper, which was never published, deals with 500 versions . . . he had 57 still births, 11.4%. In his last report he had 1130 deliveries in a year of which 938 were by version and 100 by Caesarean section . . . A man who delivers 1130 women in one year must shorten the hours of labor."

"A letter from Vienna (by E. I. Tuohy): . . . Is Vienna the medical center it was before the war? Is it a good place for Americans to go now? The old morgue in the Krankenhaus is cleaner and sprightlier than it has ever been before, thanks to the Rockefeller Foundation. Erdheim is sectioning and demonstrating on the same old stone table used by Rokitansky. The gross pathology opens up like the pages of a beautifully bound book . . . While many courses are offered in English . . . it is far better to blunder badly into the German language. It is a virile speech and has already withstood most heroic punishment at the hands of some of us . . ."

"Conditions simulating an acute leukemia . . . In 1915 Hall reported to the Royal Society of Medicine a case resembling acute lymphatic leukemia with recovery in a young adult. In 1920 Sprunt and Evans described six similar cases. Sprunt and Evans cases were all young adults between the ages of 23 and 29. The striking clinical features are these:

"1. An acute febrile disease, usually with a local infectious, but non-suppurative process.

"2. Enlargement of the lymph glands of the neck, axillae, or groins, or combination of these, and enlargement of the spleen.

"3. A relative increase in the mononuclear white cells, either with or without a moderate leucocytosis, less than 20,000 usually.

"4. The occurrence of certain white cells difficult to classify, but which are generally assigned as

lymphoblasts.

"5. Recovery."

All of these Fifty Year Club members have given a lifetime of service to the State of Minnesota and have earned the gratitude of its citizens. The undisputed leader of this class, of course, is Owen Wangensteen, the maker of professors of surgery, the outstanding surgical educator of our time. The professor's professor. The medical class of '22 will not be forgotten.

Reuben Berman, M.D.
Editor

Sigmoidal Complications of Left Ovarian Enlargement

With their practical and usual pragmatic approach to surgical problems, Drs. Lee and Associates* suggest a practical point, i.e., to remove the left ovary instead of the right if there is a choice when doing pelvic surgery. Diverticulosis and or diverticulitis of the sigmoid colon should always be considered in the differential diagnosis of left adnexal masses, especially from the fifth decade of life on. General and gynecological surgeons are well advised to consider neoplasms and inflammatory processes and endometriosis with left lower quadrant abdominal and left adnexal masses, and to be prepared for injury to and involvement of the sigmoid colon and the appropriate surgical therapy for such.

Mancel T. Mitchell, M.D.
Minneapolis, Minnesota

*Lee, R. A. et al.: Sigmoidal Complications of Left Ovarian Enlargement, Minnesota Med 55:565, 1972.

Cover Photograph

"Mazatlan Sunset"

This cover picture is a 35 mm. transparency taken from the top floor of the Hotel Playa Mazatlan on Las Gaviotas Beach Mazatlan, Mexico.

This area is noted for its beautiful sunsets and is one of Dr. L. B. Folsom's and his wife's favorite vacation spots.

Dr. Folsom is certified in Occupational Medicine and practices at the Northwest Industrial Clinic. He is on the staff at Metropolitan Medical Center and Fairview Hospital.

Surgical Treatment of Vascular Ring

Vascular ring has long been recognized as a serious congenital malformation that may cause repeated pulmonary infections and death in early infancy. Less commonly, patients with a vascular ring will remain asymptomatic until adult life. Drs. Thompson and Read[12] reported a case of an adult with right aortic arch and anomalous left subclavian artery which produced a ring effect in combination with left ligamentum arteriosum. As the authors indicated, their repair was similar to that proposed for patients with the reverse situation, that is, a left arch and an anomalous right subclavian artery. Arterial continuity was restored by anastomosis of the proximal end of the subclavian artery to the ipsilateral carotid artery.

The anomaly of right aortic arch, aberrant left subclavian artery, and left ligamentum constitutes a relatively rare form of vascular ring. We have encountered only one such case, that of a 10-month-old boy, in a series of 19 patients with vascular ring who underwent corrective surgery.[1] In addition to late onset of symptoms, the authors' patient was somewhat unusual in that his presenting symptom was dysphagia. Most patients with vascular ring who are symptomatic in infancy and childhood have predominating symptoms related to respiratory distress and repeated pulmonary infections. It is clear, however, that some patients may become symptomatic only in adult life and that the first symptom may be dysphagia. In some instances, this may result from aneurysmal dilation of the aberrant vessel.[2,3]

In principle, reconstitution of subclavian artery blood flow is desirable in order to prevent intermittent claudication of the involved arm or neurologic symptoms from the development of a subclavian steal syndrome.[4,5] No cases of severe distal ischemia have been reported from division and suture of an aberrant subclavian artery at its origin from the aorta, although rare cases of gangrene of the arm have been reported after the use of a normally situated subclavian artery for other purposes.[6,7] Similarly, a significant subclavian steal phenomenon has not been reported after division of an aberrant subclavian artery, but it is reasonable that such could occur, as symptomatic subclavian steal has developed after Blalock-Taussig anastomoses.[8]

The authors pointed out that only a few aberrant right subclavian arteries are symptomatic. It is interesting that none of the cases in our series[1] involved an aberrant right subclavian artery with a descending left thoracic aorta, in contrast to many series in the literature. There are many uncertainties about the symptoms this anomaly may cause. It does not form a true ring, with the exception of the rare form in which right ligamentum arteriosum or right patent ductus arteriosus develops. Of 106 patients at the Mayo Clinic,[9] only five had dysphagia, but in none of these five was dysphagia attributed to the aberrant right subclavian artery. There must be other anomalies to cause such symptoms, as suggested by Klinkhamer.[10] A vascular ring effect is common, however, when there is an aberrant left subclavian artery and a right descending thoracic aorta (authors' case), since the left ligamentum arteriosum connecting to the left pulmonary artery completes a ring.

The authors disconnected the subclavian artery from the aorta through a left thoracotomy and then anastomosed the distal end of the artery to the left common carotid artery. From the technical standpoint, this procedure may be simpler than reattaching the subclavian artery to the ascending aorta in its usual location. A similar technique is commonly employed for revascularization of a subclavian or innominate artery with proximal occlusion, in which a graft is sewed end-to-side to the ipsilateral common carotid artery and end-to-side to the involved vessel distal to the obstruction. Temporary complete or partial occlusion of the carotid artery, however, carries a small but distinct hazard from cerebral complications caused by the interruption of normal cerebral blood flow. This hazard is not present when a side clamp is employed on the ascending aorta for anastomosis.

The authors have demonstrated again that it is not essential, as has often been recommended in the past, to approach an aberrant subclavian artery through the pleural space in which the descending thoracic aorta is situated. This is similar to our experiences of satisfactory exposure of the junction of an aberrant subclavian artery

with the aorta through either pleural space, when it has been necessary to enter one particular side for other considerations. For example, an aberrant right subclavian artery arising from a left descending thoracic aorta was satisfactorily exposed through a right thoracotomy when it was necessary to perform lobectomy simultaneously because of a solitary pulmonary nodule in the right middle lobe.

If reanastomosis of the subclavian artery is being considered, however, it is preferable to enter the pleural space on the same side as the artery. Performance of the entire operation through a single incision would seem to be preferable to the two-incision operation described by Siderys.[11] Therefore we would consider the authors' contention sound: that the patient with an aberrant right subclavian artery and left arch should be approached through a right thoracotomy and the divided subclavian artery anastomosed to the right common carotid artery (or ascending aorta) and that patients with a reverse situation should have a similar procedure conducted from the left side.

Gordon K. Danielson, M.D.
Rochester, Minnesota

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Decision Making in Scoliosis

THE MOST COMMON pitfall in the treatment of scoliosis is the failure to recognize the insidious progression of a spinal curvature in a growing adolescent while she is being "observed" by her physician.

The article by Winter and Moe* (also pioneers in the treatment of scoliosis, although they modestly neglected to include themselves in this category in their article) stress several important points worth re-emphasizing.

1. Even though a curvature is mild in a growing patient, evidence of progression of the curve is indication for treatment with the Milwaukee brace.

2. Once growth has ceased in the older adolescent, the Milwaukee brace is ineffective in obtaining lasting correction.

3. Observation of the patient's curve, without treatment, is indicated only in those patients in whom a curvature is mild and does not progress. Lack of progression must be established by x-rays made in the erect posture at regular intervals through the period of spinal growth.

4. There is no place for exercise as the sole form of therapy for scoliosis. Exercises improve posture but do not reduce curves or prevent progression.

5. Spinal fusion is indicated for those curves which are too severe to be controlled by the Milwaukee brace.

A. J. Bianco, Jr., M.D.
Rochester, Minnesota

*Winter, R. B. and Moe, J. H.: Idiopathic Scoliosis. Minnesota Med 55:529, 1972

Letters to the Editor

Dear Editor:

WAS I GLAD to see SNOMed (deriv of SNOP) commended by AHW MD in MINN MED of JUN. WHAT a SCOOP. I am sure SNOP was gratified at its CAP raising reception by AFIP in DC and by ACS INC in NY. But what a shame for the CIOMS; a good thing it seems that a generous UNESCO came through with the $ so that they could sire IND after all. However, although Topography (T) was clear and Eitology (E) easily explicable, Function (F) seemed + −, even when called X Y. May I suggest that before more Committees for Rephrasing, Elucidation and Testing of International Nomenclatures (CRETINS) are produced an IUD is placed in UNO WHO, ie AMA CMITS (Amy Schmidt (Ger) (Adapt)).

I remain in IBM-convenient form,
SOC SEC NO 206 42 4151

A. H. Woodward
Rochester, Minnesota

Dear Editor:

It was with great pleasure that each of us had the opportunity to see, all at one time and in one place, the dedication to Dr. Rice. Since each of us has known him and worked with him and has had the opportunity to consider him a friend as well as a physician to whom we would like to refer patients, we feel that MINNESOTA MEDICINE has helped us crystalize many of the things we did not know about this very modest citizen in our midst.

Elizabeth B. Jerome, M.D.
Nancy R. Lund, M.D.
Maxine O. Nelson, M.D.
Barbara H. Subak, M.D.
Shirley J. Peterson, R.N.
Minneapolis, Minnesota

Request for Physican's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers have received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the Association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Because of limitation of space, pictures oriented horizontally are preferred. All pictures will be returned if identified with the name and address of the physician. Please submit your pictures as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 375 Jackson St., St. Paul, Minnesota 55101.

Farrell Stiegler, M.D.
Cover Editor

In Appreciation

The many fine technical exhibitors who participated in the exhibit during the recent Minnesota State Medical Association Annual Meeting are deserving of our recognition and a hearty "thank you!" Not only did the presence of these exhibits enhance the educational quality of our meeting, the support provided by our exhibitors is essential to the continuance of our traditionally outstanding scientific program.

The firms listed below participated in our 1972 Annual Meeting exhibit and we voice a collective expression of our sincere appreciation. May we also suggest that you retain this listing and express your personal appreciation when their representatives call upon you.

George B. Martin, M.D.
President

Abbott Laboratories
Allied Medical Audit Control
American Linen Supply Company
Ames Company
C. F. Anderson Co., Inc.
Astra Pharmaceutical Products, Inc.
Blue Cross-Blue Shield-MII
Bureau of Credit Control, Inc.
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Casualty Indemnity Exchange
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Norelco Dictation Systems
North Star Consultants, Inc.
Northwestern National Life Insurance Company
Office Interiors, Inc.
Organon, Inc.
Ortho Comfort Stores
Parke, Davis & Company
John A. Peters & Associates
Physicians & Hospitals Supply Company
Piper, Jaffray & Hopwood
Port Industries, Inc.
Riker Laboratories, Inc.
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Sandoz Pharmaceuticals
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3M Business Products Sales, Inc.
Ulmer Pharmacal Company
The Upjohn Company
Warner-Chilcott Laboratories
Waters Instruments, Inc.
Harold J. Westin & Associates, Inc.

dvertisement

"The history of science, and in particular the history of medicine...is... the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

–George Sarton, from "The History of Medicine Versus the History of Art"

Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

13.3%
Yes, it would be useful.

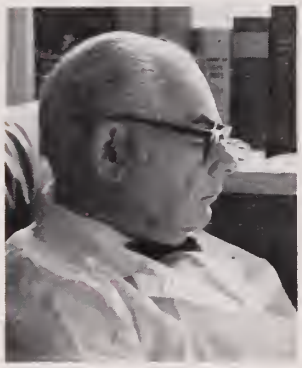
86.7%
No, it would not be useful.

Dialogue

Would it be useful in clinical practic to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

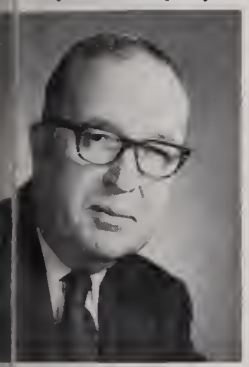
I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy in practice can really determined.

The Bureau of Drugs suggested the package sert as a possible mean communicating informa on relative efficacy of d to the physician. I find objectionable, since I not believe the physi should have to rely on source for final scien truth. There is also a p tical objection: Since physicians actually pense drugs, they sel see the package insert any event, I would m tain that the physi should know what dru wants and why without pending on the govern or the manufacturer to him.

Undoubtedly, physic are swamped by exces numbers of drugs in s e therapeutic categories. I am well aware that m drugs within such c gories could be elimin without any loss, or haps even some profit the practice of medic e But, in my opinion, nei r the FDA nor any o er single group has the ex tise and the wisdom ne sary to determine the "drug of choice" in l areas of medical practi

Maker of Medicine

eth G. Kohlstaedt, M.D.,
Vice President,
Medical Research,
Eli Lilly and Company



In my opinion, it is not
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time the new drug
u l be labeled "the drug
h oice." But as addi-
o l clinical experience is
c nulated, new evidence
a become available.
a r, it may be apparent that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audiovisual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

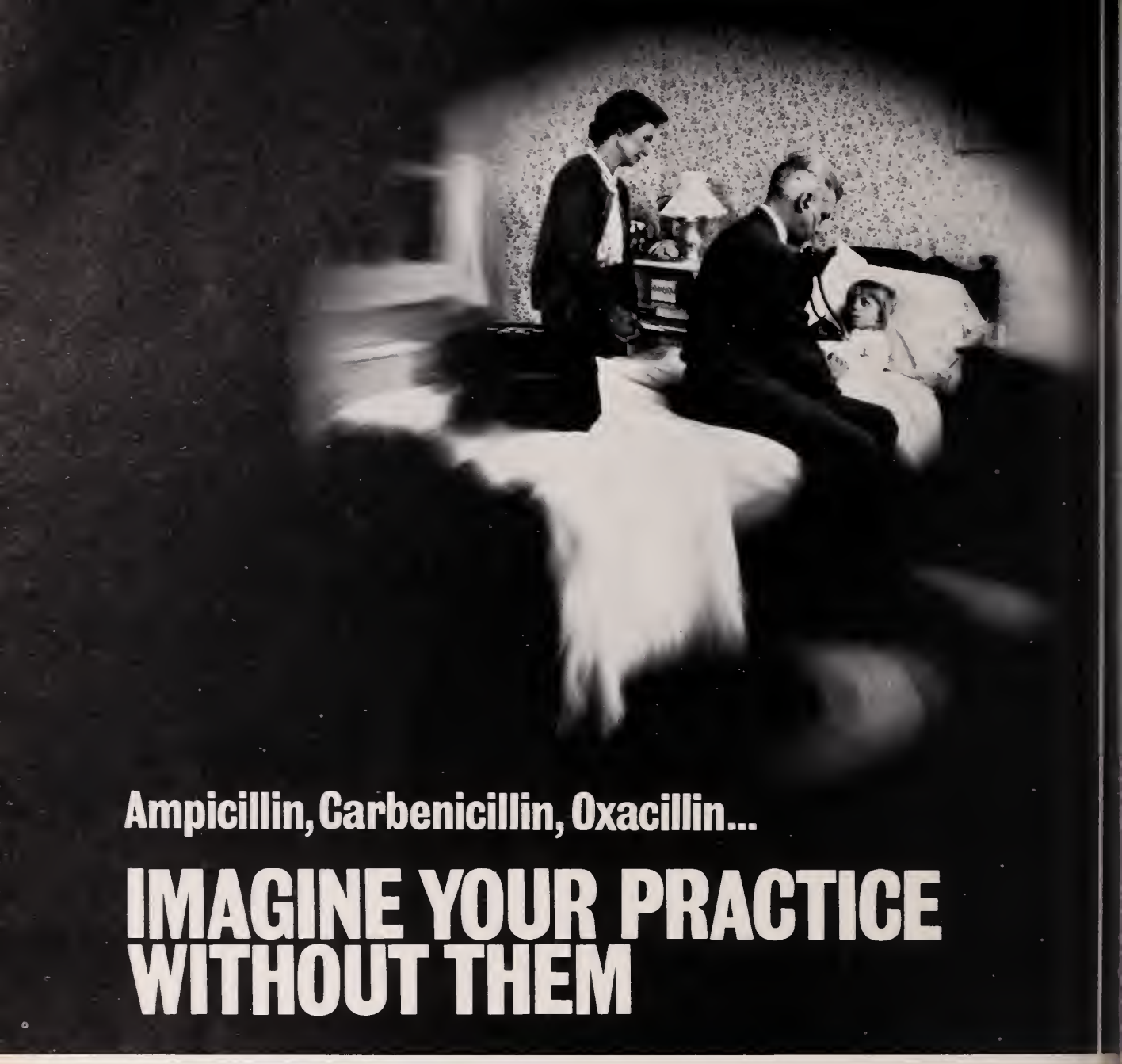
Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use — information that the pharmaceutical manufacturers must begin to provide if government regulation of *"drugs of choice"* is to be avoided.

Opinion & Dialogue

What is your opinion, doctor?
Send us your comments on the above issue.

P·M·A

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Fifty Years of Faithful Service

Alvin G. Athens, M.D.

Dr. Alvin G. Athens specialized in ophthalmology and otolaryngology. Born in Fairmount, Indiana, 1887, he attended school in Summitville, Indiana; receiving his A.B. degree from De Pauw University, 1915 and obtained his medical education at Johns Hopkins University, graduating in 1919. He took postgraduate work at Pennsylvania Post Graduate School, at the New York Eye and Ear Hospital in New York City, and at the Chicago Polyclinic. Dr. Athens served in Buhl, Minnesota, for two years, for 36 years in Duluth, and retired in 1960.

J. Richards Aurelius, M.D.

Dr. J. Richards Aurelius has one phase of his medical experience which for a long time has been of great interest and satisfaction to him. This is his association with the detection of tuberculosis and the role of medical and public health organizations in the exciting period of this disease from about 1925 to the present.

During this period Dr. Aurelius saw a wide range of therapy from simple bed rest, then pneumothorax, thoracic surgery to a large group of antibiotics to a period now of a remarkably specific control, possibly in the range of eraxication.

A roentgenologist, certified by the American Board of Radiology, Dr. Aurelius received his M.D. degree from the University of Minnesota and served as a Fellow in radiology at the Mayo Foundation. In 1928, he became an assistant instructor in the Department of Radiology, University of Minnesota, and later served as clinical professor retiring in 1966.

Alfred N. Bessesen, Jr., M.D.

Alfred N. Bessesen, Jr., born in Minneapolis September 27, 1896, followed the medical tradition of his parents, A. N. Bessesen, M.D., and Florence Holland Bessesen, M.D. He received all his degrees—B.S., B.M., and M.D., the latter with distinction, from the University of Minnesota, where he was elected to Sigma Xi and received the Geist prize for research in anatomy. He served his internship at City-County Hospital, St. Paul, and the University of Minnesota Hospitals.

Dr. Bessesen's primary hospital affiliation throughout his career has been with Methodist Hospital, Minneapolis, where he was president of the medical staff in 1950. He served in World Wars I and II as commander medical corps, U. S. Naval Reserve, with duty in the Philippines.

Dr. Bessesen pioneered in the medical care of alcoholics in the early 1940's and introduced the use of Disulfiram (Antabuse) in October, 1951, when it was first available in the U.S.

He has been a lifelong supporter of varsity athletics at the University of Minnesota, particularly through the Williams Scholarship Fund.

Dr. and Mrs. Bessesen have two children, Mrs. William G. Heegaard, Alexandria, Minnesota, and Alfred N. Bessesen, III, Columbus, Ohio, and seven grandchildren.

Ferdinand W. Bofenkamp, M.D.

Dr. Ferdinand W. Bofenkamp is a general practitioner with 48 years of service in Luverne and Rock County. Born in Ellsworth, he attended Dubuque University, Dubuque, Iowa. Doctor Bofenkamp received his M.S. degree from St. Louis University Medical School, St. Louis, Missouri, and served his internship and residency at St. John's Hospital, St. Louis, Missouri.

Lewis R. Bouma, M.D.

Dr. Lewis R. Bouma, surgeon, was born in Chicago. He is a graduate of the Universities of Iowa, Iowa City, and Minnesota. Doctor Bouma interned at Mounds Park Hospital, St. Paul, and did postgraduate work at New York College, New York. He served on the surgical staff of Bethesda Hospital, St. Paul.

Ruth E. Boynton, M.D.

Dr. Ruth E. Boynton was born and grew up in La Crosse, Wisconsin. After three years of premedical education at La Crosse State University, she attended the University of Wisconsin, for the first two years of medical school, receiving the B.S. degree in 1918. In 1921 received the M.D. degree from the University of Minnesota Medical School.

Her entire professional life was spent in the field of College Health and Public Health. After a few years on the staff of the Students Health Service, during which time graduate work was taken leading to an M.S. degree in Public Health, she became Director of the Division of Child Hygiene of the Minnesota Department of Health, a position held for four years.

In 1927 Dr. Boynton returned to student health work for one year at the University of Chicago, and from 1928 to retirement in 1961, she was at the University of Minnesota. From 1936-1961 was Director of the University Health Service and Professor of Public Health at the University of Minnesota.

From 1939 until 1961 she was a member of the State Board of Health, serving as President for two years.

Dr. Boynton was recipient of a Fulbright Research Award for six months study of Student Health Services in Britain in 1951.

In addition she was recipient of the following awards: Edward Hitchcock Award of the American College Health Association; Harrington Award given by the Minneapolis Junior Chamber of Commerce for service in public health and Albert J. Chesley Award of the Minnesota Public Health Association.

Herbert Boysen, M.D.

Dr. Herbert Boysen was born at Alvord, Iowa, March 4, 1898. He moved to Sioux City, Iowa in 1910 and graduated from high school in 1916. He attended the State University of Iowa where he took his premedic work and graduated from the College of Medicine in 1922. His internship was at the Receiving Hospital in Detroit, Michigan, 1922-23. In October, 1923 he was married to Minnie L. Olson and they have one son, Dr. James F. Boysen, a pediatrician at Sioux City.

Dr. Boysen has practiced at Truman, Minnesota 1923-26, at Welcome, Minnesota 1926-41 and at Madelia, Minnesota since that time. He has been secretary of the Blue Earth Valley Medical Society for the past 27 years.

Leo C. Culligan, M.D.

Dr. Leo Culligan's premedic work was taken at St. Thomas College and at the University of Minnesota, graduating in Medicine in 1922 and interning at Ancker Hospital in St. Paul, July 1922 to July 1923. He was accepted as a fellow in surgery at the Mayo Foundation July, 1923 and returned to St. Paul in 1926 where he practiced in surgery with his brother John until 1930.

The depression days of 1930 were spent at the Veteran's Hospital, Department of Surgery until 1943. In 1943 he took over the offices of Dr. Arthur Strachauer in association with Dr. Frank Hirshfield, Doctor Strachauer having retired about that time. Since that time he has been in practice in surgery doing the major portion of his work at St. Mary's Hospital.

In 1951 Dr. Culligan was Chief of Staff at St. Mary's Hospital, and in 1952 was elected president of the Minneapolis Surgical Society.

In 1927 he was married to Leone Dennis, from Marquette, Michigan, a former nurse from St. Mary's Hospital at Rochester. Eight children and 51 grandchildren are the result of this union.

He is still actively engaged in the practice of surgery in Minneapolis.

Raymond J. Dittrich, M.D.

Dr. Raymond J. Dittrich, as an orthopedic surgeon, has done extensive studies on lumbo dorsal fascia. Doctor Dittrich did postgraduate work at the University of Iowa, Iowa City; Los Angeles Orthopedic Hospital; and Gillette State Hospital, St. Paul, after receiving his M.D. degree from the University of Minnesota. He is certified by the American Board of Orthopedic Surgery and is a Fellow in the American Academy of Orthopedic Surgeons.

Benjamin Anton Dvorak, M.D.

Dr. Benjamin Anton Dvorak devotes his services to the field of surgery and general medicine. He obtained his B.S., M.B., and M.D. degrees from the University of Minnesota where he also took his postgraduate work in surgery and gynecology. He was on the surgical staff at Iowa State University Hospital, Ames, Iowa, in 1923 and 1924. Later he came to Minnesota as an instructor at the University Medical School and joined the staffs of St. Mary's and Deaconess Hospitals in Minneapolis.

In addition to his career in medicine, Dr. Dvorak had a career in athletics. While at Iowa State University he coached the football team 1923-24 and played football at the University of Minnesota in 1917, and 1920; pro football for the early NFL the first year of its organization, 1921. He captained and quarterbacked a championship football team while with the Eastern Army Ambulance Corps in 1918. In 1919 for several months, he played professional baseball with Louisville in the American Association, until returning to Medical School. For some years, he played trombone with the University of Minnesota Symphony Orchestra and the Minneapolis Symphony Orchestra, and was solo trombonist with the University of Minnesota Concert Band, 1915 to 17. Dr. Dvorak was born at New Prague, Minnesota, in 1896.

Edward T. Evans, M.D.

The Evans family made a large contribution to medicine; Dr. Evans' father was a Physician and Surgeon; one brother entered the field of internal medicine; another brother, the field of neurosurgery. Dr. Evans was born at LaCrosse, Wisconsin, in 1900. He received his education at Notre Dame University, the University of Wisconsin, and graduated from Harvard Medical School in 1922. Postgraduate training at the Boston Floating Hospital and Boston City Hospital in pediatrics, obstetrics, gynecology and general surgery. He did his Orthopaedic postgraduate work at the Hospital for Ruptured and Crippled in New York City, the Continental Clinics and under Sir Robert Jones in Liverpool and London. Dr. Evans was since 1927 a member of the teaching staff of the University of Minnesota in the Department of Surgery in Orthopaedics and now is an Emeritus Professor (Clinical) of Orthopaedic Surgery. He was Chief of Resident training in Orthopaedics at the Veteran's Hospital at Fort Snelling, as well as serving as a consultant there.

He was an infantry lieutenant in World Wars I and II, served over four years as Chief of Orthopaedic Surgery of the 26th General Hospital (U. of M.) in England, North Africa and Italy and at Billings General Hospital at Fort Benjamin Harrison, Indiana with the rank of Lt. Colonel. He was awarded the Legion of Merit in 1946. In 1957 he was consultant for the Surgeon General to the Far East Command.

He was president of the Clinical Orthopaedic Society, and the Association of Bone and Joint Surgeons and twice president of the Min- Da- Man Orthopaedic Society.

Aaron Friedell, M.D.

His mother's oft repeated suggestions in childhood was: (1) "Make knowledge accumulation your principle aim in life. With knowledge and experience you develop wisdom (most important)." (2) "Silver and gold can blindfold the eyes of wise men."

The above ideas were put to a hard test when as a high school junior Dr. Friedell after school worked for the Universal Film Company. One day he was given a film package, a first run for Red Wing Theater, to be delivered to the train (five blocks away). Although he ran all the way he missed the train.

In his pocket he had $2.10 and there upon took a taxi for the St. Paul Railroad Station and his mission was successful. With ten cents left he returned by streetcar to find the office group all upset (two and one half hours for my return—at 6:00 p.m.).

The manager called Dr. Friedell the following day and offered him a job to be trained as an assistant booker at a starting salary of $25.00 a week. The offer was not accepted as it would interfere with his education and the accumulation of knowledge.

Dr. Friedell is still at it—aiming to accumulate knowledge and that all elusive kernel of wisdom.

Isadore M. Goldberg, M.D.

Dr. Isadore Goldberg has been in active practice of medicine in Minneapolis until the last five years and since then he has limited his practice to insurance medicine.

Throughout this period he has maintained offices in the Minneapolis loop. His avocations include tennis, and he still has a hard serve to return. Dr. Goldberg is married to Blanche (Halpern). They have two children, Arthur and Dr. Stanley.

Lawrence Gowan, M.D.

Dr. Gowan was born at Ardoch, North Dakota. His father was a pioneer settler in the Red River Valley. He graduated from Park College, Parkville, Missouri, following which he entered Medical School at the University of Minnesota.

After interning at the University Hospital, he was granted a Teaching Fellowship in Nervous and Mental Diseases. Under Dr. McKinley's direction he carried out a research problem in Postencephalitic Paralysis Agitans. He received an M.S. in Nervous and Mental Diseases from the University of Minnesota in June, 1925 and was elected to Sigma Xi.

In July, 1925, Dr. Gowan entered private practice in Duluth and in 1934 he persuaded St. Mary's Hospital to establish a special department for the care of the mentally ill. He was certified by the American Board of Psychiatry and Neurology in both Neurology and Psychiatry in May 1939.

In 1937 he helped establish the Duluth Mental Hygiene Clinic and was for several years its Medical Director. In 1948 Dr. Gowan set up the Douglas County Guidance Center in Superior, Wisconsin and was its Medical Director on a part time basis until June 1971.

He served as Chief of Staff of St. Mary's Hospital and Chief of the Department of Psychiatry at both St. Mary's and St. Luke's Hospitals on several occasions.

His hobbies are gardening and fishing and he works every day hoping to put in another five years in active practice.

Bayard T. Horton, M.D.

Dr. Bayard Taylor Horton was graduated from the University of Virginia School of Medicine in 1922. After some tenure as professor of biology on a college faculty in Virginia he came to the Mayo Graduate School of Medicine in 1925, where he later was named associate professor of medicine. In 1929 he was appointed to the staff of the Mayo Clinic, a post he occupied until he retired in 1958. In 1940 he was appointed head of a section of clinical investigation. With his colleagues Dr. Horton was able to identify and describe two new disease entities: temporal arteritis (Horton's disease) and "Horton's syndrome" (histaminic cephalgia which now are standard terms in medical dictionaries. The two diseases are unrelated. Currently he is Director of Medical Research at the new Walter O. Boswell Memorial Hospital in Sun City, Arizona.

Frank J. Kucera, M.D.

Dr. Frank J. Kucera was born in McLeod County, Hutchinson Township, September 24, 1894 and attended country school, the Hutchinson High School, graduating in 1913, and the University of Minnesota from 1915 to December 15, 1921. He served on the staff of St. Barnabas Hospital for 49 years and has been an active staff member of Methodist Hospital since 1959.

He married Alma Foss of Minneapolis, 50 years ago, and they have three children and six grandchildren. Dr. Kucera loves to travel, fish and spends a great deal of his time in his gardens.

Robert F. McGandy, M.D.

Dr. Robert F. McGandy throughout his career as a surgeon, has been an active member of his local medical society and the Association. He was president of the Hennepin County Medical Society in 1950. He has been on the Association's Judicial Committee on Automotive Injuries and presently is on the Insurance Liaison Committee. Doctor McGandy was certified by the American Board of Surgery in 1945 and is an emeritus clinical assistant professor of surgery at the University of Minnesota. He is a past president of the Minneapolis Surgical Society, founding member of the American Burn Association and a Fellow in the American College of Surgeons. He was graduated from the University of Minnesota.

Maurice W. McInerny, M.D.

Dr. Maurice W. McInerny was born in Minneapolis, May 21, 1898, where he has been a lifetime resident. In active practice since graduation, he received his B.S., M.B., and M.D. from the University of Minnesota and interned at City and County Hospital, St. Paul and at St. Mary's Hospital, Minneapolis.

Married Helen Marshman, graduate nurse of St. Mary's and plans to celebrate his golden wedding anniversary, January 10, 1973. At the present time there are three daughters, nine grandchildren and one great granddaughter to make life quite worth while. Work volume has been curtailed but he has no thought to complete retirement except by public demand. He has devoted his career to general practice and hospital work in surgery and obstetrics.

Paul F. Meyer, M.D.

Dr. Paul F. Meyer has been a general practitioner and surgeon in Faribault since 1926. He is currently on the staff of St. Lucas Hospital and in 1950 was president of St. Lucas-Deaconess Hospital Medical Staff. During his years in Faribault, he has been county physician, health officer, and a member of the county board of health.

Hamilton Montgomery, M.D.

Dr. Hamilton Montgomery was graduated from the Harvard Medical School in 1922 and came to Rochester, Minnesota, in 1925, as a second-year fellow in the Mayo Graduate School of Medicine. In 1929 he was appointed to the staff of the Mayo Clinic as a consultant in dermatology, and from that time until his retirement in 1959 was privileged to devote himself to dermatohistopathology as well as clinical dermatology. He co-authored and authored three editions of *Diseases of the Skin*, with Dr. Oliver S. Ormsby; and in 1967 his two-volume *Dermatopathology* was published. His holiday hours are spent in his sailboat on the Mississippi River as a member of the Coast Guard Auxiliary.

Dr. Montgomery was vice president of the American Dermatological Association, Inc., in 1958, president of the Chicago Dermatological Society in 1938, a founder and first president of the Dermatopathological Society (1962), vice president of the Society for Investigative Dermatology, president of the Minnesota Dermatological Society and an honorary member of the New York Dermatological Society and of European dermatological societies.

C. L. Oppegaard, M.D.

Dr. C. L. Oppegaard, well-known specialist in ophthalmology and otolaryngology was awarded the Association's 1962 Distinguished Service Award. He was council chairman, 1954-60, president-elect, 1960, president, 1961, councilor and member of the House of Delegates for several terms. He was also a member of the Committee on University Relations. Doctor Oppegaard was a graduate of the University of Minnesota where he interned and completed post-graduate work. He was a Fellow of the American College of Surgeons and a member of the American, Minnesota and North Dakota Academies of Ophthalmology and Otolaryngology. Doctor Oppegaard spent his years of active practice serving Crookston.

Arthur B. Roehlke, M.D.

Dr. Arthur B. Roehlke has devoted his years of practice to Elk River. Educated at the University of Minnesota, he interned at the University and Miller Hospitals. With the Association, he served on the Committee on Trauma and was delegate and alternate delegate to the House of Delegates. He is also a past president and former secretary-treasurer to the East Central Minnesota Medical Society. He remains in practice and is surgeon for the Northern Pacific Railway.

Robert Rosenthal, M.D.

Dr. Robert Rosenthal was born in Austria and had his entire schooling in that country, including medical education. He graduated from the medical school of the University of Vienna in 1922 after having spent three and one-half years in World War I. After a half year residency in Internal Medicine at the Vienna General Hospital, one year residency in a Children's Hospital and some postgraduate work in Berlin, he came to this country late in 1923. He took his State Board Examination in 1924 and has since practiced pediatrics in St. Paul. From 1926 on he did some teaching at the pediatric department of the University as assistant demonstrator and assistant professor in pediatrics, but was inactive for a number of years before being placed on the emeritus list.

For about twenty-five years Dr. Rosenthal served on the staff of Ancker Hospital in the pediatric department and for many years was active in the Greater St. Paul Health Council. In 1961 he served as vice-president of the Ramsey County Medical Society and over half of this time as acting president.

For many years he was chairman of the Historical Committee of the Minnesota State Medical Association and during that period coordinated the medical history of many counties in Minnesota and authored a few of his own.

Dr. Rosenthal has been a member of the medical staff of the Family Nursing Service of St. Paul since 1924, being its oldest member in years of service.

Raymond J. Spurzem, M.D.

Dr. Raymond J. Spurzem is a general practitioner and has been medical advisor to the Anoka County Selective Service Board for 35 years. He has served as advisor to the County Welfare Board and as deputy county coroner. A graduate of the University of Minnesota, Doctor Spurzem interned at the University Hospitals, served on the staff of Eitel Hospital, Minneapolis, as local surgeon for the Great Northern and Northern Pacific Railways and assistant physician at the Anoka State Hospital.

Walter C. Stillwell, M.D.

Dr. Walter C. Stillwell, a surgeon for many years at the Mankato Clinic, is a graduate of the University of Minnesota and did postgraduate work there and at the University of Vienna. He is a member of the American College of Surgeons, International College of Surgeons and the American Society of Abdominal Surgeons. For several years, he was on the Association's Public Health Education Committee.

E. J. Tanquist, M.D.

Dr. E. J. Tanquist, general practitioner, was honored as one of Minnesota's leading practitioners by the Minnesota Academy of General Practice in 1953. In 1928, he built the Douglas County Hospital, approved by the American College of Surgeons. Doctor Tanquist is a diplomate of the International Academy of Proctology. Outside his medical practice, he has spearheaded many community projects. In 1972, he was elected an outstanding Kiwanian and given a life fellowship in the Kiwanis International Foundation. Doctor Tanquist remains in active practice with his son.

Owen H. Wangensteen, M.D.

A biographical sketch of Dr. Owen Wangensteen will appear in an early issue.

"What's a Sawbones?" inquired Mr. Pickwick, not quite certain whether it was a live animal, or something to eat.

"What! Don't you know what a Sawbones is, sir?" inquired Mr. Weller. "I thought everybody know'd as a Sawbones was a Surgeon."

"Oh, a Surgeon, eh?" said Mr. Pickwick, with a smile.

"Just that, sir," replied Sam. "These here ones as is below, though, ain't reg'lar thorough-bred Sawbones; they're only in trainin'."

"In other words they're Medical Students, I suppose?" said Mr. Pickwick.

Sam Weller nodded assent.

"I am glad of it," said Mr. Pickwick, casting his nightcap energetically on the counterpane. "They are fine fellows; very fine fellows; with judgments matured by observation and reflection; tastes refined by reading and study. I am very glad of it."

"They're a smokin' cigars by the kitchen fire," said Sam.*

*Charles Dickens, Pickwick Papers, Chapter XXX (1836).

if skin is infected, or open to infection...

choose the topicals that give your patient–

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin®-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.

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When you select this familiar antibiotic for IV infusion you have available a broad dosage rang that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections.

In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomyc hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in wate But when 4 grams or more per day is given, Lincocin should be diluted in n less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

ifections caused by susceptible strains
pneumococci, streptococci, and
aphylococci, including penicillin-
sistant strains. Staphylococcal strains
sistant to Lincocin (lincomycin
ydrochloride, Upjohn) have been
covered. Before initiating therapy,
lture and susceptibility studies should
performed. Lincocin has proved
luable in treating patients hyper-
nsitive to penicillin or cephalosporins,
ice Lincocin does not share
tigenicity with these compounds.
owever, hypersensitivity reactions
ve been reported, some of these in
tients known to be sensitive to
nicillin.

ell tolerated at infusion site: Lincocin
travenous infusions have not
oduced local irritation or phlebitis,
ien given as recommended. Lincocin
usually well tolerated in patients who
e hypersensitive to other drugs.
evertheless, Lincocin should be used
utiously in patients with asthma or
gnificant allergies.

patients with impaired renal function,
e recommended dose of Lincocin
ould be reduced to 25—30% of
e dose for patients with normal
dney function. Its safety in
egnant patients and in infants
s than one month of age has
t been established.

ncocin may be used with other
timicrobial agents: Since Lincocin
stable over a wide pH range, it is
itable for incorporation in
ravenous infusions; it also may be
administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rash, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hr. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin 250 to 500 ml of 5% glucose in distilled water or normal saline has produced only local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

For additional product information, consult the package insert or see your Upjohn representative.

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Case Report

Sino-Orbital Aspergillosis

Report of a Case and Review of the Literature

H. H. ZINNEMAN, M.D.*

USUALLY ASPERGILLOSIS is encountered in the human as an opportunistic infection in individuals with debilitating diseases, immune deficiences or recipients of immunosuppressive or antimetabolic drugs. It may appear as a saprophyte, presenting as a "fungus ball" in pulmonary cavities. Involvement of the nasal mucosa, maxillary and ethmoid sinuses without extension to the orbit may occur in individuals with unimpaired general health.[1-5] Maxillo-orbital aspergillosis has also been observed in otherwise healthy patients.

Case Report

A 46-year-old divorced Caucasian male had been subject to chronic alcoholism, which had led to chronic pancreatitis. It also manifested itself radiologically with pancreatic calcifications. A mild diabetes mellitus, secondary to this condition, had never led to diabetic acidosis or other complications, in spite of the patient's unwillingness to observe a dietary regimen. The patient presented himself because of orbital pain and rapidly declining vision of the right eye. He was an unkempt man of poor general and particularly oral hygiene. There was a continuous offensively smelling mucosanguineous discharge from the right naris. The right lower turbinate appeared swollen and gangrenous. There was a marked right ocular proptosis. Funduscopic examination showed a pale right retina. A trickle of erythrocytes could be seen in the main retinal artery. It stopped during the examination, at which time the patient stated that he could not see anything with the right eye. At the beginning of the funduscopic examination he had been able to distinguish light from darkness.

Laboratory Findings

Initial laboratory findings were as follows: *Urinalysis:* Specific gravity 1010, pH 8.0, acetone 0, glucose 3+, protein 0, microscopic examination of the sediment 0-5 WBC/HPF. *Blood:* Hb 9.0, Hct 26.5, RBC 2,910,000, MCD 7.2, WBC 9.720 (78% PMN, 22% mononuclear cells). Blood sugar 115mg/100 ml, BUN 16 mg/100 ml, Na 139, K 4.1, Cl 100, CO_2 28 meq/100 ml, cholesterol 169 mg/100 ml, SGOT 18 U. Total serum bilirubin 0.2 mg/100 ml, alkaline phosphatase 11.3 KAU.

Assuming that he was dealing with maxillo-orbital mucormycosis, the attending physician initiated intravenous therapy with Amphotericin B in doses gradually increasing to 50 mg daily. Surgical removal of the gangrenous tissue from the lower turbinate and most of the mucosa from the right maxillary sinus provided specimens of mucous membrane for histologic examination and was followed by a decrease of the exophthalmos (Figure 1). Histologic preparations of the mucosa showed chronic inflammatory reaction surrounding hyphae, which were interpreted as Mucor (Figure 2). Cultures had not been incubated at that time. While the patient received intravenous therapy with Amphotericin B to a total of 2 gm, his general status improved. His diabetes mellitus never offered a problem and was satisfactorily controlled by dietary measures. He was discharged from this hospital, but returned after 14 months, because a fistulous drainage had established itself in the right canine fossa, discharging malodorous serosanguineous exudate (Figure 3). A radial Caldwell-Luc procedure yielded additional specimens of mucosa, which were cultured. Histologic preparations were similar to the ones obtained previously, and cultures yielded

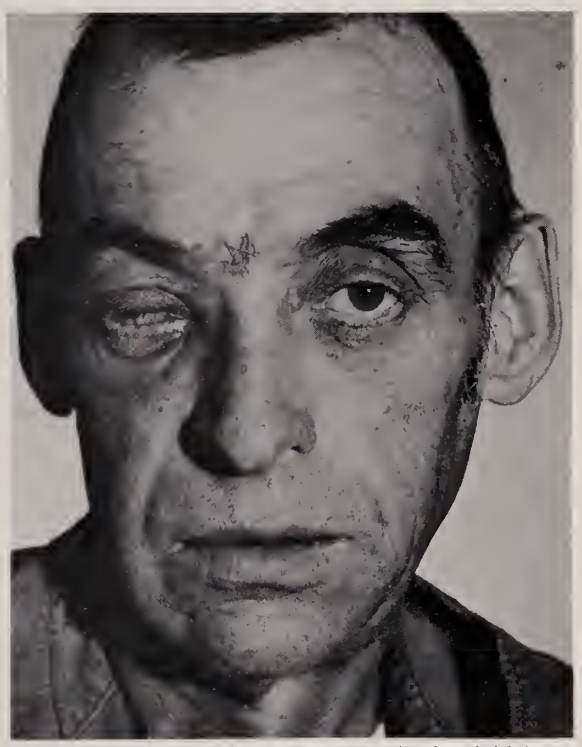


Fig. 1—Orbital involvement one week after initial surgical intervention and intravenous therapy with Amphotericin B. The proptosis has decreased but palpebral and periorbital edema is still prominent.

*Medical Service of the Minneapolis Veterans Administration Hospital and the Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota.

Aspergillus flavus (Figure 4). There also was a small growth of *Nocardia asteroides*. Postoperatively the sinuses were irrigated with solutions of Amphotericin B. The fetor disappeared and subsequent cultures failed to grow *A. flavus* or *N. asteroides*. There has been no recurrence during 18 months of clinical follow-up observation.

Comment

Deep mycosis is one of the causes of rapidly developing exophthalmos. The geni Mucor and Aspergillus figure prominently in this clinical picture. Whereas sino-orbital mucormycosis has been observed mainly in individuals with debilitating diseases or conditions, such as diabetic acidosis, alcoholic cirrhosis, uremia, leukemia and neoplasms, similar involvement by Aspergillus usually has been observed in otherwise healthy persons.



Figure 2—Mycelial hyphae in a section of mucosa from the right maxillary sinus. H & E stain magnification X 400.

Aspergillus may involve only a maxillary sinus.[1-6] From there it may extend to the orbit, causing pain, exophthalmos and frequently amaurosis due to invasion and occlusion of the ophthalmic artery.[7-12] The Table lists the reports

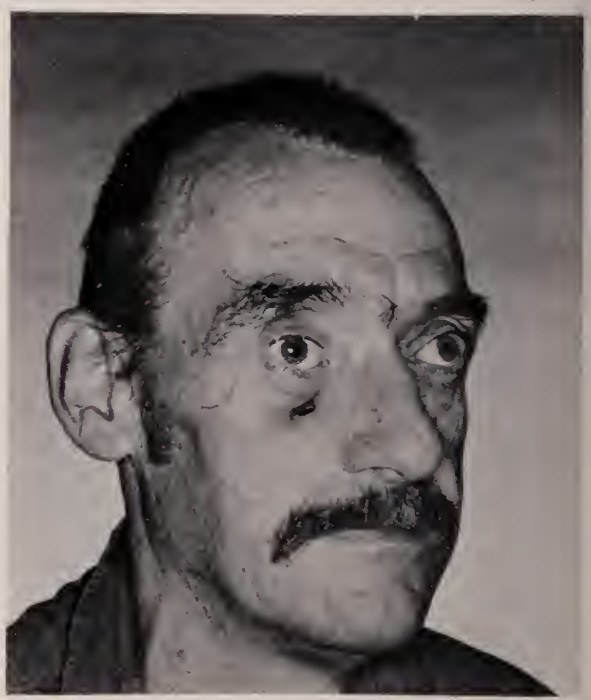


Fig. 3—Spontaneous drainage from the right orbit through a fistula in the canine fossa.

TABLE

Previously Reported Cases of Aspergillosis of Nose, Sinuses and Orbit

Author & Year	No. of Cases	Identif	Aspergillus Species	Other Diseases	Involvement: Nose	Involvement: Maxillary Sinus
Wright 1927	2	Culture	A. flavus	No	Yes	Yes
Adams 1933	1	Culture	A. fumigatus	No	Yes	Yes
Kelly 1934	7	Culture	A. fumigatus	No	Yes - 7	Yes - 4
Montreuil 1955	1	Culture	A. fumigatus	No	Yes	Yes
Anderson 1956	1	Culture	A. fumigatus	No	Yes	Yes
Arnaud 1957	2	Culture	A. fumigatus	No	Yes	Yes
Grunberg 1959/60	1	Histol	Aspergillus	No	Yes	Yes
Weller 1960	1	Culture	A. flavus	No	Yes	Yes
Savetsky 1961	1	Histol	Aspergillus	No	Yes	Yes
Bailey 1961	1	Culture	A. flavus	No	Yes	Yes
Hora 1965	1	Culture	A. flavus	No	Yes	Yes
Milosev 1969	17	Culture	A. flavus	No	Yes - 17	Yes - 17
Crivelli 1970	1	Histol	Aspergillus	No	—	—

of 24 cases, where this development took place. None suffered an underlying debilitating disease. Aspergillosis of the nose and a maxillary sinus was found in all patients except one. The patient without maxillary sinus involvement was reported by Crivelli.[13] A circumscribed aspergilloma at the optic foramen was the cause for his unilateral amaurosis. There was no proptosis. The clinical picture was consistent with that of a meningioma of the right optic foramen. Surgical exploration found and removed a pea-sized aspergilloma at the optic foramen, between optic nerve and carotid artery. General involvement of the orbit with exophthalmos and proptosis was the rule, where involvement of the orbit resulted in a space-occupying mass.[7-12] Therapy with antifungal agents was used in seven cases (see Table) and found disappointing. In one instance, where it represented the only means of therapy[10] the patient died subsequent to an extension of the process into the brain. In the remaining six patients antifungal therapy was considered futile, and surgical treatment resulted in improvement or cure. On the other hand, whenever surgical treatment was employed, either as sole method of treatment (28 cases), or in combination with antifungal therapy (six cases) the therapeutic results were better. Of the 34 surgically treated patients only one failed to improve, and one died. *A. flavus* was encountered more frequently than *A. fumigatus* as the pathogenic agent.

The case under discussion also was caused by *A. flavus*. The patient's diabetes mellitus was a sequence of chronic pancreatitis and never had led to complications. It was easily controlled by dietary regimens. In this respect this patient is comparable to other patients with sino-orbital aspergillosis without underlying debilitating diseases. Confirming the experiences of others, our treatment with Amphotericin B did not effect lasting results, whereas subsequent surgery was curative. It is of interest that spontaneous drainage through a fistula in the canine fossa had been



Fig. 4—Culture on Czapek agar produced a greenish-yellow growth. Conidia and conidial heads are greenish-yellow, sterigmata are short and stubby. Magnification X 440.

TABLE (Continued)

Orbit	Proptosis	Visual Defects	Therapy	Result	Miscell
Yes	Yes	Blindness	X-ray	Not followed	
Yes	Yes	Yes	KI, surgery	Recovered	Canine fossa fistula
—	—	—	Surgery	Recovered	
—	—	—	Surgery	Recovered	
—	—	—	Surgery. - KI	Not improved	
—	—	—	Surgery. Crystal Violet	Recovered	
—	—	—	Surgery	Recovered	
Yes	Yes	Yes	KI, Amphot. Surgery	Palliative results	Temporal fistula
—	—	—	Surgery	Recovered	
Yes	Yes	Blindness	Amphot. KI, griseofulvin	Died - ext. to brain	
Yes	Yes	Blindness	Amphot., Pimar., Surgery	Recovered	
Yes	Yes - 15	15 blind	Surgery	1 died, 16 cured	
Yes	—	Blind	Surgery	Recovered	

noted in a previous case.[8] In another patient[9] spontaneous drainage from the involved orbit established itself in the temporal region, anterior to the right ear.

The experience from this patient and from review of the literature suggests the following:

1. Sinomaxillary mycosis occurring in an otherwise healthy individual is most likely due to an Aspergillus species.
2. The species involved is most likely *A. flavus* or *A. fumigatus*.
3. Antifungal therapy used exclusively is unsatisfactory. Its value as supportive therapy is uncertain.
4. Surgical removal of the involved tissue is the most promising therapy, with or without supportive antifungal therapy.
5. Surgical intervention is particularly urgent in orbital aspergillosis, where the eyesight is still preserved.

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It's the Law

No Malpractice in Treatment of Hip Fracture

A 28-year-old patient sustained a fracture of her left hip as a result of an automobile collision. She was examined by her family physician and a surgeon. Xrays were taken under the supervision of a radiologists and they indicated an impacted fracture of the left femoral neck. An open reduction was performed, a Smith-Peterson nail was inserted. Xrays immediately following surgery indicated good position and alignment with the fracture and good position of the nail.

Xrays over the next several months indicated deterioration of the head of the femur. A third consultation was sought, the nail was removed and the patient was treated for several months in a spica cast. Subsequently, a girdle stone operation was carried out resulting in shortening of the leg and some stiffness.

The court ruled that no negligence had been exhibited, that the standard of care was satisfactory and that the only detectable error on the part of the physician, if it was indeed an error, was not informing the patient of the possibility of the aseptic necrosis of the femoral head at the time of the original injury.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Bryant v. Rankin, 332 F. Supp. 319 (D.C., Iowa, Aug. 11, 1971)
The Citation 25:1, April 15, 1972.

The Chronic Alcoholic in a Small Community Hospital

JAMES J. GARBER, M.D.*

DETOXIFICATION OF the acutely intoxicated alcoholic in a general hospital setting has previously been reported,[1-8] demonstrating the feasibility of alcoholic detoxification on a general medical floor. Such a program in a small community hospital has not, however, previously been described.

Hospital treatment of the chronic alcoholic seems indicated for three reasons. First, alcoholism is a multisystem disease[9-19] and requires a general medical evaluation which can often be best accomplished in a hospital. Second, treatment of the various alcoholic withdrawal syndromes,[20] which can be severe and unpredictable, may require hospital care. Last, removal of the alcoholic from his drinking environment to begin rehabilitation is frequently necessary.

The present study was undertaken to establish the workability of such a program in a small community hospital.

Materials and Methods

All patients admitted for alcoholic detoxification to the medical service of the Olmsted Community Hospital from August 1967 to September 1970 were included in this study. The Olmsted Community Hospital is an 85-bed general hospital. During the period of this study there were 10,630 admissions.

Admission policy was patterned after the guidelines of the American Medical Association's Commission on Alcoholism and Drug Dependence for admission of such patients to a general hospital.[21]

Incidence

Of the 10,630 admissions, 85 were for alcoholic detoxification. Seventy-seven patients were involved in the 85 admissions. These represented 0.8% of the total hospital admissions. Seventy patients were admitted once, six patients twice, and one three times. There were 2.3 admissions per month. The average hospital stay was 6.8 days; the average stay for a medical patient was 7.4 days.

Age and Sex

Sixty-seven patients were men and 18, women, a ratio of 3.5 to 1. The average age at time of admission was 50.3 years, approximately the same for both sexes.

Occupation

In the group there were 14 priests, which indicates a bias introduced by the opening in Rochester, during the study period, of Guest House, Inc., a treatment center for alcoholic priests. There were 14 housewives, 12 construction or maintenance workers, seven farmers, four unemployed persons, three executives, one physician, one lawyer, one nurse, and 25 patients with other occupations. Seven of the patients in the study were retired.

*Internist, Olmsted Medical Group, Rochester.

Presented as part of the seminar "The Treatment of the Hospitalized Alcoholic" sponsored by the Mayo Clinic and the Zumbro Valley Medical Society.

Withdrawal Syndromes and Complications

Withdrawal syndromes included tremulousness in 73 patients, hallucinosis in seven, and delirium tremens in five.

Medical complications included hepatic coma in three patients, seizure in one, and cardiac arrest in one (with successful resuscitation). One patient developed severe cirrhosis, and one patient bled from esophageal varices. Four patients died —two in hepatic failure, one with severe cirrhosis, and one of an intracranial hemorrhage.

Associated Medical Problems

Laboratory studies revealed significant abnormalities in 75 of the 85 patients. These included evidence of liver disease in 61 patients, six of whom had liver biopsies. The remainder had abnormal liver function tests or hepatomegaly, or both. Thirty-seven patients had abnormal electrocardiograms, non-specific repolarization abnormalities representing the most frequently seen change. Twenty-two showed evidence of a lipid abnormality: elevated cholesterol, triglyceride, or abnormal lipoprotein electrophoretic patterns. Fifteen had abnormal chest x-rays, one of whom showed active tuberculosis by culture; 12 were diabetic; 12 had some urinary abnormality such as a urinary-tract infection, proteinuria, or depressed creatinine clearance; and seven showed evidence of obstructive lung disease.

Other abnormalities included anemia, electrolyte imbalances, evidence of alcoholic myopathy, peptic ulcer disease, and a colonic polyp. Only six patients required psychiatric consultation, one was diagnosed as schizophrenic, and the remainder had neurotic disorders.

Nursing Care Problems

Extra nursing care was required for 12% of the patients. The conditions necessitating the extra nursing care included incontinence, terminal liver disease, pneumonia, and delirium tremens. One patient required extra care for a Blakemore tube and two required cardiac monitoring. Twenty-seven per cent needed a moderate degree of nursing care for such problems as occasional incontinence, mild confusion, frequent requests for medications, bed care for personal hygiene, and help with eating and walking. The remaining 61% required only minimal care: they fed themselves and took care of their own personal hygiene. Five patients left against medical advice and five confused patients wandered outside their rooms or attempted to climb over side rails, requiring additional nursing vigilance. Two patients needed restraints. Most were in private rooms. There were no management problems that necessitated male nurses or aides.

Economic Liability

In general, the patients or their insurance companies paid the hospital costs promptly. Of the 77 patients, 79.2% paid their bills in full or were paying regularly; or payment was by public welfare or Medicare. We received partial payment of 10.4% of bills, which included those for patients whose insurance company or Medicare paid a portion of the hospital costs though the patient had not contributed subsequently. About 6.5% of the bills were written off or put into collection accounts.

Discussion

When this study was undertaken, there was some apprehension: among the hospital medical staff, that they would be inundated with admissions for chronic alcoholism; among the nursing staff, that they would be faced with difficult nurs-

ing problems (both professionally and physically); and in administration, that this would represent a financial liability. It is apparent that the alcoholic patient constitutes none of these problems.

In addition, the high association of general medical disorders with chronic alcoholism was confirmed. These medical problems have often necessitated hospitalization and, in the past, alcoholic patients have been admitted without recognition of the basic disease process. The diagnosis of alcoholism was, therefore, neglected; and so was its therapy.

Though no long-term alcoholism-treatment program exists at the Olmsted Community Hospital, an attempt is made in each case to initiate a contact with the Alcoholism Information Center and Alcoholics Anonymous. Patients are started on a program using the facilities available in Rochester, are referred to an alcoholism treatment center for a more intensive rehabilitation program, or, if necessary, are committed for therapy at the State Hospital at Willmar, Minnesota.

It is hoped that this study will help dispel the concept of the "skid-row" alcoholic, frequently seen in a city-county hospital setting, and bring recognition of the problems of the more conventional alcoholic who lives in both urban and rural areas, spans the whole of the socio-economic scale, and whose care can be successfully managed in a community hospital.

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Cervical Cancer Mortality Study

The past several decades have witnessed substantial improvement in the overall outlook for cervical cancer patients. Presently, two-thirds or more of all squamous cell carcinomas of the cervix are diagnosed while still in-situ and at a time when the prognosis for cure, if proper treatment is carried out, approaches 100%. While the absolute number of invasive cancers of the cervix in the United States appears to have remained relatively stable for the past 20 years, during the same time the incidence rate in Connecticut has decreased by more than 40% and in British Columbia and New York by more than 50%.

Among patients with invasive cancers of the cervix, only about 50% of such cases have disease classified as "localized" at the time of diagnosis. The overall 10 year relative survival rate for patients with clinical cancers of the cervix is reported to be slightly higher than 50%.

Thus, although it would appear that efforts of the past several decades for earlier detection of cancers of the cervix have been remarkably successful in terms of reducing the incidence rates of invasive cervical cancer, and efforts for more effective therapy have been productive of improvements in long-term survival for those with cancers diagnosed after invasion has occurred, women continue to die of this disease. In fact an estimated 9,400 will die of cancer of the cervix in the United States and probably about 100 in Minnesota this year. This is not a good record for a disease that theoretically is 100% curable!

Because of the seeming availability of methods and facilities to permit almost all cervical cancers to be diagnosed and treated while early enough to be potentially curable, and because deaths from cancer of the cervix continue to occur in Minnesota as well as in the rest of the nation, a project is currently underway to study the circumstances associated with the course of the disease in each instance in which a cure was not achieved and the cancer caused the death of the patient. This study will include all deaths from cancer of the cervix reported as occurring during the period from 1 January 1971 to 31 December 1972. Areas of deficiency in diagnosis, care, and follow-up will be delineated and studied.

This cancer mortality study was undertaken by a special subcommittee functioning under the auspices of the Obstetrics, Gynecology and Maternal Health Committee of the Minnesota State Medical Association, with the joint sponsorship of the Minnesota State Department of Health, and with the approval and endorsement of the Minnesota Division of the American Cancer Society, the Minnesota Obstetrical and Gynecological Society, the Minnesota Society of Clinical Pathologists, the Cancer Committee of the Minnesota State Medical Association, the Council of the Minnesota State Medical Association, and the Northlands Regional Medical Program.

The study committee will be known as the Cervical Cancer Mortality Committee, and will be directly responsible for the conduct of the study including the formulation of a suitable protocol of items of inquiry and review of all data prior to formal presentation of periodic reports to the sponsoring organizations. The Committee will include professional persons conversant in the areas of gynecologic oncology, gynecologic surgery, radiation therapy, public health, pathology, vital statistics and in the family practice of medicine.

The study of the circumstances of each death from uncontrolled disease will be initiated by working retrospectively beginning with the physician who signed the death certificate.

The collection of data will be accomplished by suitable professional people knowledgeable and experienced in detection, diagnosis and treatment of gynecologic malignant disease. On-the-site review of physician and hospital records and interviews with involved physicians and surviving relatives will be conducted. Pathology and cytology specimens will be reviewed and modes of therapy will be evaluated.

The Cervical Cancer Mortality Committee will assemble and review the data, assess the progress of the study, and initiate modifications or improvements as indicated. At the end of the study a summary of the activities and findings of the Committee will be presented to the sponsoring groups.

The information relating to the patients studied regardless of source, will be used solely for the purposes of this Study and is held strictly confidential under Minnesota law (Subdivision 1 of Section 144.053) and is not admissible before any court or other tribunal.

Konald Prem, M.D.
Minneapolis, Minnesota

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(Continued on page 674)







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ENERAL ASSAY TECHNIQUE	"Its major disadvantage is inadequate standardization of hormonal content."[8]	Unlike desiccated thyroid U.S.P., thyroxine does not require biologic standardization to establish its potency.[2,6] Crystalline T_4 is used. Purity is verified by paper chromatography. Content of tablets is standardized by weight.
LINICAL RESPONSE	"T_3 and T_4 ratio varies according to gland source. Fluctuations in response can occur. Potency can vary."[3]	"Sodium levothyroxine has been extensively used with satisfaction and is widely held to be superior to (desiccated) thyroid."[7] "There are well documented examples of patients who failed to respond satisfactorily to desiccated thyroid but subsequently responded to (sodium-1) thyroxine."[4]
REDICTABILITY	Failure of thyroid U.S.P. treated patients to show clinical improvement and/or lack of correlation in clinical findings to thyroid function test results has been frequently discussed in the literature.[8,9,10,11,12,13,14,15,16] Regardless of which factor or factors accounts for this phenomenon the fact remains that discrepancies do occur.	Test results predictably elevated. ". . . oral potency of this material is attested to by a uniformly good clinical response corroborated by a prompt and sustained increase in the serum PBI levels."[16]

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Unscored 5 mcg.	N.A.	N.A.	unscored ¼ gr.	¼ gr.	0.025 mg.
N.A.	½	½	unscored ½ gr.	½ gr.	0.05 mg.
25 mcg.	1	1	unscored 1 gr.	1 gr.	0.1 mg.
N.A.	N.A.	N.A.	N.A.	1½ gr.	0.15 mg.
50 mcg.	2	2	unscored 2 gr.	2 gr.	0.2 mg.
N.A.	3	3	unscored 3 gr.	3 gr.	0.3 mg.
N.A.	N.A.	N.A.	unscored 5 gr.	5 gr.	0.5 mg.
N.A.	N.A.	N.A.	N.A.	N.A.	Injectable 500 mcg.

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*Equivalents shown are chemical, and do not take into consideration individual patient variables. Clinical effect is approximate and should be monitored when converting a patient to SYNTHROID. This is particularly important in patients previously on desiccated thyroid. In these patients, lower doses of SYNTHROID may produce the same metabolic effect.

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Precautions: As with other thyroid preparations, an overdosage may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Disease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

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(Continued from page 669)

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Meetings

The 32nd Annual AMA Congress on Occupational Health will be held at The Drake Hotel in Chicago, September 11-12, 1972. Contact Dr. Henry F. Howe, AMA, 535 North Dearborn Street, Chicago for further information and reservations.

Southern Minnesota Medical Association Meeting, September 23, 1972, in Austin, Minnesota.

The 10th Annual Cancer Chemotherapy Conference will be held at the University of Wisconsin, Madison, on September 6-8. The program will include a review and forward look at anti-cancer therapy, multiple drug therapy of solid tumors and leukemias, the role of x-ray therapy, immunology and virology in the treatment of cancer. For information contact Dr. G. Ramirez, 714C University Hospitals, Madison, Wisconsin 53706.

Fracture Conference

Comminuted Intra-Articular Distal Radial Fractures

Dr. Einer W. Johnson, Jr.:

Comminuted intra-articular fracture of the distal end of the radius can be a challenging problem to the orthopedist.

Case 1

Dr. Charles P. Fina:

A 23-year-old man fell on his outstretched left hand, sustaining an injury to the distal end of the radius. He had a "silver-fork deformity" but no impairment of his nerve or vascular functions. The Xray (Figure 1A) showed an obvious deformity of the distal portion of the radius, with comminution and intra-articular extension of the fracture.

Dr. Johnson:

Some comminuted distal radial fractures penetrate the radiocarpal joint. This one had a fracture line that went directly into the joint and, like many fractures of this type, the fracture line was more visible after reduction than before. Note the disruption of the articular cartilage.

Dr. Fina:

The fracture was manipulated under local anesthesia, with longitudinal traction and counteraction. It was brought out to length, and good restoration of the radial angle was accomplished (Figure 1B). The volar tilt was about neutral. The patient did well in his cast.

Dr. Johnson:

The lateral fragment of the radius was a large single piece. The comminution occurred toward the ulnar joint side, and the joint line was well restored by the reduction. Significantly in these cases, the largest fragment in the comminution will almost always be on the lateral side of the distal fragment.

Dr. Fina:

The comminution in this case involved the medial fragment, which is true in up to 85% of comminuted fractures of the distal radius. This type was described by Scheck[1] and is caused by forcing the lunate into the distal end of the radius.

The patient's cast was changed at three weeks. Position was maintained, and another cast applied for two additional weeks. The Xray at six weeks after fracture (Figure 1C) showed a good anatomic result. The patient still had some residual discomfort in his wrist but had good dorsiflexion and volar flexion. There was a slight limitation of ulnar and radial deviation, but supination and pronation were full.

Dr. Johnson:

Case 1 represents a moderately comminuted fracture of the distal radius in which reduction and its maintenance were satisfactory. The patient had some loss of motion and some pain two and one-half months after fracture.

Case 2

Dr. Fina:

A 38-year-old man fell six feet from a ladder onto his outstretched hand, with immediate pain in the wrist and paresthesias in his thumb and index finger. Radiographic examination revealed (Figure 2A) comminution of the radius distally, as well as intra-articular extension of the fracture.

Dr. Johnson:

Just as in Case 1, there was comminution at the level of the distal radio-ulnar joint, the almost completely intact lateral portion of the distal fragment, and the invasion of the joint by the fracture line. However, this patient was treated differently.

Dr. Fina:

Closed reduction was attempted under local anesthesia, and a fair reduction was obtained. However, as the patient had severe pain and paresthesias in the distribution of the medial nerve, the position of the wrist had to be altered. When this was done, the position of the fragments was lost. He was taken to the operating room the following day and underwent release of his carpal canal because of severe and persisting carpal-tunnel symptoms. At the same time, a Kirschner wire was inserted into the metacarpal at the thumb, a cast was applied, and traction was exerted through the metacarpal of the thumb.

Dr. Johnson:

The reason for the skeletal fixation was to try

Fracture Conference April 14, 1969.

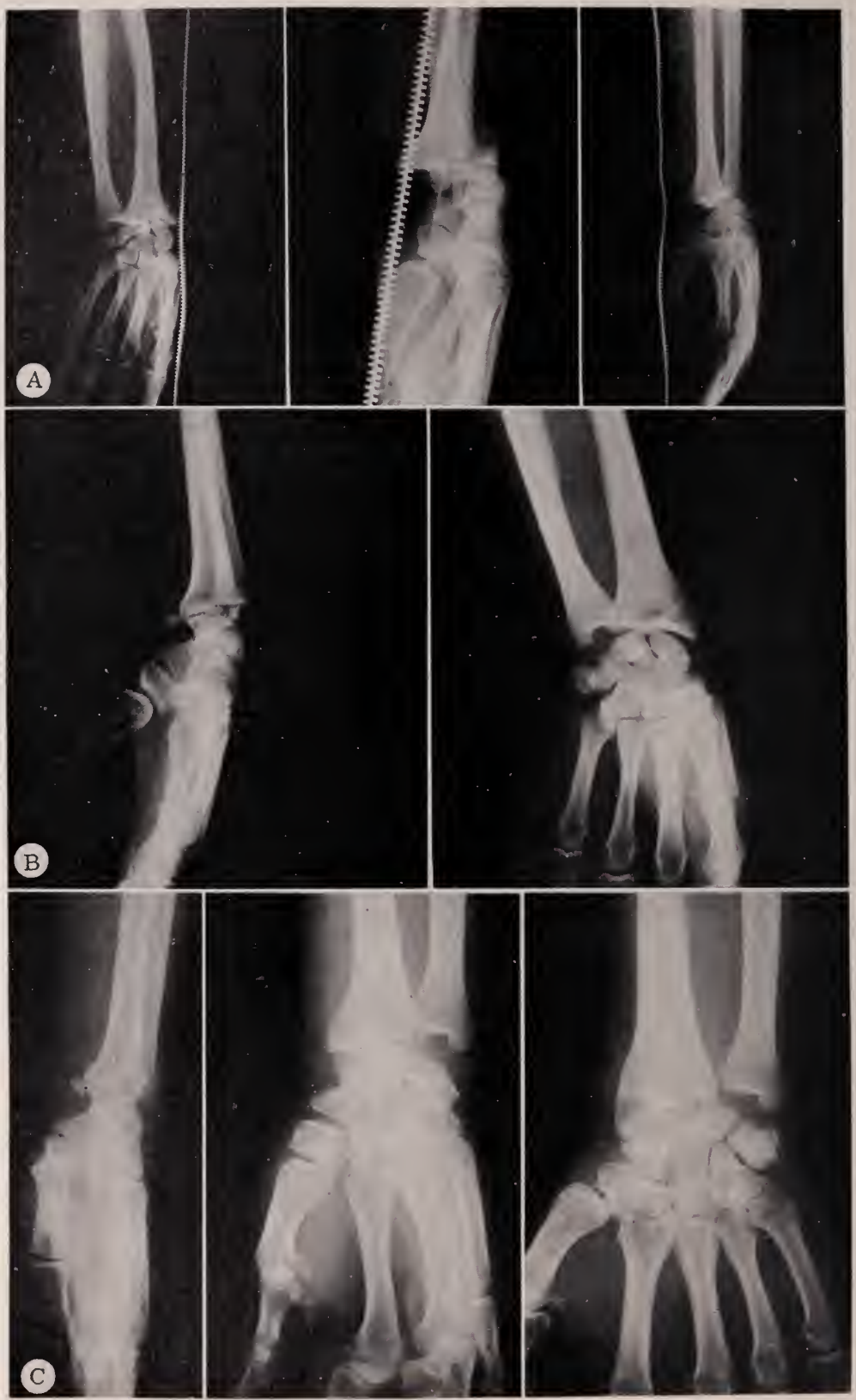


Fig. 1—Comminuted, intra-articular fracture of distal radius. (A) Sept. 1, 1968. Anteroposterior and lateral views show significant medial comminution, reasonable intact lateral cortex, and dorsal shift of carpus. (B) Sept. 18, 1968. Anteroposterior and lateral view show excellent reduction, with maintenance of radial length, radial and volar angles. (C) Oct. 14, 1968. Anteroposterior and lateral views show final healed position, with excellent anatomic result.



Fig. 2—Comminuted, intra-articular fracture of distal radius. (A) Dec. 15, 1968. Initial anteroposterior and lateral views reveal severe comminution, intra-articular extension, and dorsal shift of carpus. Comminution is more medial than lateral. (B) Dec. 18, 1968. Anteroposterior and lateral views reveal loss of reduction (shortening, dorsal tilt, and shift) despite skeletal traction. Patient had subsequent manipulative reduction in an attempt to gain an improved anatomic position. (C) Feb. 20, 1969. Final anteroposterior and lateral views show loss of volar angle and radial length, with good radial angle. This was an excellent functional result.

to maintain length and keep the fracture from collapsing. The wound healed per primum.

Dr. Fina:

The patient was brought to the operating room five days later, and the wound was inspected and found to be healing. Pin traction (Figure 2B) was kept in place, and "sugar-tongs" splints were applied. However, four days later, the position had slipped and length was lost. His radio-ulnar joint was remanipulated again under general anesthesia.

Dr. Johnson:

Our efforts to maintain reduction and to maintain length again failed.

Dr. Fina:

Position was lost. His radio-ulnar joint was manipulated and the pins were removed at this time.

Dr. Johnson:

We agreed to accept that position. He was a young man of 38 years, and he still had satisfactory radial length in relation to the ulnar length and a reasonable angle to the articular surface of the distal radius (Figure 2C). He had a modest radial shift of the hand; but the shift was not enough to be striking, and he was happy with his result. Although the anatomic result was not perfect, the functional result was acceptable.

Case 3

Dr. Fina:

An elderly woman fell on her outstretched left hand. She had had a Colles' fracture of the same wrist 14 years before. Physical examination showed the typical deformity of the wrist. We have some Xrays showing her wrist in the reduced position. (Figure 3A).

Dr. Johnson:

There was comminution that involved the joint, a good deal of shortening, and a completely intact lateral aspect of the distal fragment. Comminution was toward the ulna, bordering on the distal radio-ulnar joint.

Dr. Fina:

In the position of palmar flexion and ulnar deviation, length was lost. The patient also had some





Fig. 3—Comminuted, intra-articular fracture of the distal radius. (A) Mar. 10, 1969. Initial anteroposterior and lateral views show severe comminution and intra-articular involvement and severe shortening. (B) Mar. 13, 1969. Anteroposterior and lateral views reveal improved length and position three days after casting. However, shortening and loss of volar and radial angles are still apparent. (C) Apr. 25, 1969. Six weeks after fracture and external skeletal pin and plaster fixation. Further collapse has been prevented, but anatomic position has not been obtained.

symptoms of median-nerve compression, although not nearly as severe as that seen in Case 2. She was operated on under general anesthesia, three days after the fracture. After longitudinal traction had been instituted (Figure 3B), skeletal pin transfixation was instituted using Kirschner wires through the second and third metacarpals and through the middle of the radius (Figure 3C). The wires were incorporated in a plaster-of-paris cast because of the severe distal comminution and collapse and because of our inability to maintain this position without some form of transfixation.

Comment

Dr. Johnson:

The types of comminuted fractures of the distal radius that we have been discussing violate the joint and are problems not only in reduction but also in maintenance of reduction, particularly maintenance of length. Dr. Fina has a few comments on the pertinent literature.

Dr. Fina:

In 1814 Abraham Colles[2] published his treatise on fracture of the carpal extremity of the radius: a fracture generally considered extra-articular. Colles[2] believed that almost all patients got a satisfactory result. Other writers[3] who examined their series of cases critically and objectively, with definite criteria, found much less favorable results. In one group, Gartland and Werley[4] noted unsatisfactory results in 68.3% of 60 patients. They also noted that the type of fracture affected the ultimate outcome. Comminution or intra-articular extension (or both) generally yielded poor results. Residual deformity had a direct relationship to poor reduction and an unsatisfactory end result. Sixty percent of their patients eventually ended up in premanipulation position if they had been treated with plaster-of-paris below-elbow casts or with "sugartongs" splints. This was particularly true when comminution and intra-articular extension were present.

In an analysis of 2,000 patients with Colles' fractures, Bacorn and Kurtzke[5] found that only 3% of patients had no disability and that there was an average disability of 24% of the entire arm. Again, residual deformity and impaired function were in direct relationship to each other. However, 96% of the patients with distal radial fractures were satisfied with their results after conservative treatment. This indicates that subjective results are much better than objective results. Again, the percentage of unsatisfactory results increases with comminution and intra-articular extension[6].

The three criteria that we should use to measure the success of the reduction are: (1) radial length, (2) radial angle, and (3) volar angle, all of which are disturbed when comminution is present. A combination rather than one single deformity causes loss of good function or form.

Adequate maintenance of reduction in a comminuted fracture can be accomplished with skeletal transfixation and incorporation into a plaster-of-paris cast. This may be one of several forms. Ulnar pinning of the distal fragment, as advocated by DePalma[7], has yielded excellent results. Cole and Obletz[8] utilized a Kirschner wire, transfixing the second and third metacarpals and the radius. Scheck[1] inserted one Kirschner wire through the second and third metacarpals near the base and placed another through the proximal end of the ulna. Both wires were incorporated in a circular plaster-of-paris cast. Finally, Carothers and Boyce[9] advocated skeletal traction through the first metacarpal for maintenance of reduction. I would tend to favor the methods of Scheck[1] and of Cole and Obletz.[8] The advantages are (1) maintenance of reduction, (2) ablation of the deformity, (3) improved function, (4) shorter rehabilitation time, and (5) avoidance of future surgery. We can anticipate satisfactory results in as many as 85% of the patients so treated.

Dr. Johnson:

In the comminuted Colles' fracture, as many as 70% of patients have poor anatomic position after reduction and without internal fixation. When you discuss Colles' fractures, do not confuse objective with subjective results. In any series, 96 or 97% of patients are satisfied with the result. Most of these are older people for whom neither cosmesis nor function is a problem; if their wrist works and does not hurt, they are satisfied. I think that it is a fallacy for the physician to analyze results by the X-ray appearance alone.

In the comminuted fracture that involves the radiocarpal joint, there are three problems: (1) loss of radial length, (2) loss of ulnar tilt, and (3) supination of the distal fragment. The average inclination of the articular surface in the anteroposterior plane should be about 23°, and there should be about 11° of volar tilt of the articular surface

on the lateral view. These, plus supination of the distal fragment, are the deformities that are caused by the fracture. Correct these and you should have a good result. However, you cannot maintain reduction in the comminuted fracture with plaster alone. Transfixation is usually necessary.

Dr. Richard S. Bryan:

The point has been made about comminution on the distal radius and its effect on the ultimate health of the radiocarpal joint. The wrist must be kept in some ulnar deviation in the plaster because this is the only way that the normal curve of the distal radial articular surface can be restored. This is the "bow" where the lunate rests.

Dr. James H. Dobyns:

The large lateral radial fragment is not always intact, as DePalma[7] has said. When this happens, we have tried DePalma's method, only to be thwarted by a split in the lateral fragment. In this case, the two-pin method would have worked well.

Dr. Johnson:

In summary, the following points can be made: 1. Comminuted fractures of the distal radius are more common than is believed. 2. The comminution is customarily near the distal radio-ulnar joint, usually penetrates the radiocarpal joint, and leaves the distal lateral aspect of the radius as one large intact fragment. 3. Although reduction is easily accomplished because of the comminution and the presence of intact ligaments and the joint capsules, maintenance of the reduced position is difficult. 4. Without some form of skeletal fixation, various degrees of loss of position are inevitable. 5. In our experience, two-pin skeletal fixation incorporated in plaster has worked well and painlessly in maintaining reduction.

Einer W. Johnson, Jr., M.D.
Charles P. Fina, M.D.
Rochester, Minnesota

Dr. Johnson is Consultant, Department of Orthopedics, Mayo Clinic and Mayo Foundation.
Dr. Fina is a Resident in Orthopedic Surgery, Mayo Graduate School of Medicine (University of Minnesota), Rochester.

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Now it is certain, that the radical heat lives in the radical moisture, but whether *vice versa*, is a doubt: however, when the one decays, the other decays also; and then is produced, either by an unnatural heat, which causes an unnatural dryness—or an unnatural moisture, which causes dropsies.—So that if a child, as he grows up, can but be taught to avoid running into fire or water, as either of 'em threaten his destruction,—'twill be all that is needful to be done upon that head.*

*Laurence Sterne, Tristram Shandy, Book V Chapter 36, 1762.

History

Chekhov, the Physician

EDMUND C. BURKE, M.D.*

PHOTOGRAPHS OFTEN show Doctor Chekhov fashionably dressed in the mode of the late 19th century with starched collar, cravat, long black coat, pince-nez glasses, and neatly trimmed goatee. He was six feet tall, thin, almost gaunt, sandy-haired, hazel-eyed, and serious in appearance. It was said that there was "no cast to his eye of the fiery revolutionary." His nature was modest and unpretentious. The nearly 600 articles and four famous plays† he wrote attest to an incredible amount of work for a life of only 44 years; such an outpouring represents an article every other week for 25 years. In addition this young man who died at 44 was a physician. When could he have found time to practice medicine and what kind of practitioner was he? How did he regard medicine as a career? How did his medical background influence his writing?

The career of Chekhov, the physician, is little known because it was so eclipsed by his literary brilliance.

The Family

Anton was the second oldest in a family of five boys and a girl.[1] He was born, in 1860, in Tagenrog, a grubby little port town on the Sea of Azov, near Rostov. His father, while possessing some talent as a choirmaster and musician, was a small shop owner and a tyrant as a parent. Anton, with his brothers, had to work in the store, do his lessons at night, and arise early in the cold, dark morning to sing in church services. He stated later in life that his childhood was no childhood. There was talent in the family, to be sure, inasmuch as his siblings became authors or teachers and one became an artist, albeit an alcoholic. None of the children embraced religion in later life, a reaction predictable under the circumstances.

When the father's business failed, the family moved to Moscow where Anton joined them at the time he was ready to enter medical school. Clues to his nature and temperament can be found in his childhood. He loved the theater and proved to be so skillful at mimicry that he amused his boyhood friends with his antics. He wrote, directed, and acted in comic plays of one or two acts. He was truly a comic, possessed of a rollicking sense of humor. This same frivolity pervaded his early writings. He employed humor rather than ridicule; he was satiric but not sardonic.

Medical Education and Early Practice

Chekhov was fascinated by Doctor Shrempf, a village physician who treated him for a serious illness, at age 15, which may have been tuberculous peritonitis. Chekhov's mother provided him with much encouragement to pursue medicine as a vocation and to help support the family during his medical days, he wrote short articles, most of which were comic sketches. During these years (1880-1884) he wrote nearly 300 under the pseudonym, Antoshe Chekonte.[2]

Anton graduated from the University of Moscow in June 1884 and went to the Chikino Hospital as a practicing physician. His first patients had a bad tooth, dysentery, and a stomach ailment, respectively, and these cases earned him a total of 14 rubles in fees. He promptly blew all this in a party for his friends. This love of friends and gaiety was typical of his life. On one occasion, when faced with a screaming child in need of a minor operation, he was forced to summon a senior colleague because he did not feel equal to the situation.

As a rural physician he was confronted with festering sores, diarrhea, and tapeworms as well as the poor diet and ignorance of the peasants and a dull village life. This routine did little to challenge his great talents. He did express the belief, however, that the practice of medicine seemed a surer way to support himself than literature. After trying two weeks at a locum tenens in Zvenigorod he was happy to escape to Moscow where he hung out his shingle.

*Mayo Clinic and Mayo Foundation: Department of Pediatrics, Rochester.

†The Seagull, Uncle Vanya, The Three Sisters, and The Cherry Orchard.

Reprint requests address to: Dr. E. C. Burke, Mayo Clinic, Rochester, Minnesota, 55901.

In the winter of 1884 he experienced the first hemorrhage from his throat (pulmonary) which was a prelude to his death 20 years later from tuberculosis. Like many physicians he refused to consult his medical colleagues (nearly 13 years elapsed before he placed himself completely under medical care).

In Moscow he had many literary acquaintances who imposed on his medical knowledge but paid him little or nothing in fees. His interest in medicine inclined toward the scientific aspects and at one time he considered writing a thesis for a higher degree. The meagerness of his income was a result of his inability to charge patients for service rendered. A lack of money and the need to support his family were still concerns in his early days. He was not wasteful in money matters but he often entertained most hospitably.

The following summer in Chikino he treated hundreds of peasants for minor ills for a total income of one ruble. He would write and practice medicine in the morning, hunt in the afternoon, and write and practice again in the late afternoon and evening. In one of his letters in 1887, he mentioned having attended a thousand patients during the previous year.[3]

He stated[4,5] that medicine was his lawful wife and literature was his mistress; when he would grow weary of one he would spend the night with the other. His story "Name Day Party" was based on an obstetric case and proved to be very popular with women for its accurate depiction of the problems and the anguish of childbirth.

Growing restless, he hit on the idea of traveling across Siberia in the spring of 1890 to the prison colony on the island of Sakhalin to investigate the living conditions of the prisoners, a journey which proved to be very hazardous. He spent the months of July through October collecting data through interviews. On file in the Moscow Lenin Museum are 10,000 cards, each of which has 13 entries, attesting to the thoroughness of his investigation. Of course, he had to have official sanction for this visit and undoubtedly he had some clerical help. The results of this study, published in 1893, were impressive and this work has been termed a shining example of a research thesis. The incredibly horrible conditions which existed were described so vividly by Chekhov that he was able to bring about some prison reforms.

Melikhovo

For seven years (1891-1898) Chekhov found a happy and congenial home at his 500-acre estate in Melikhovo. Anton personally planted many fruit trees, planned the garden, and became endeared to the peasants who flocked to him with their ills. In 1892 he had accepted a position as a member of the Sanitary Commission[5] responsible for a section of the province threatened by a cholera epidemic. He showed great executive ability in organizing the hospital, and he often drove about the territory day and night to see patients. He built three schools in Melikhovo and gave his moral and financial support to a new journal, *The Surgical Chronicle*. He also proposed, supported, and supervised the building of a community library.

The following letter[6] (translated from Russian by the author) from Chekhov's sister, Marya, is evidence of Chekhov's avowed pride in his vocation in medicine.

Yalta
6 October 1953

Dear Comrade Geizer!

I completely support your view that Anton Pavlovich always was interested in the practice of medicine and never turned away from the work of a physician. Truly, he esteemed his social position as a physician. You may also have read in the recollections of many contemporaries how Anton Pavlovich always maintained that he was a physician. You may even state that on moving from Melikhovo to Yalta, Anton Pavlovich gave as a gift almost his entire library to the city of Tagenrog, taking with him to Yalta only his most beloved books at the same time taking all of his medical books, even those lectures which he at one time studied at the University. And, if you read his letters, remember how he worked for preservation of the journal "Surgery" etc.

Are you acquainted with the book of Khizhnyakov "Chekhov as a Physician"? There the theme is the same as you have taken. (The book was published five years ago.)

I wish you success. Good health.

Yours.
M. Chekhov

Yalta

In 1898 because of his failing health and the insistence of his physician, he sold the Melikhovo estate and built a villa on the hills above Yalta. This home is now a museum dedicated to him and his life. He continued to devote time to the sick, many of whom were consumptives from all over Russia. He took an active part in education and for his efforts he was awarded the Stanislav medal. He raised money and directed efforts to

construct and equip a tuberculosis sanatorium. He worked in his gardens where he was often photographed with his dogs in his moments of relaxation. The last six years of his life were very fruitful despite his illness—during this period he wrote five plays, one of which was *The Seagull*, staged by Stanislavsky in the Moscow Art Theatre.

Very little is known of his romantic interests in life because there is little or nothing in his letters to indicate more than a passing interest, let alone a major romantic attachment. Olga Knipper, by then a famous actress in the Moscow Art Theatre, consented to marry Anton in May 1901. The couple lived together very little since Olga's theatrical career kept her in Moscow, and Anton could rarely leave Yalta because of his failing health.

In January 1904, Chekhov attended the successful first performance of *The Cherry Orchard* in Moscow. He was obliged to return to Yalta after a few months. For his deteriorating health it was recommended that he travel to Badenweiler in the Black Forest. Three weeks later he died, on July 2, 1904, at the age of 44. His wife survived him until 1958.

The Nature of His Works

Chekhov's early works were frivolous and light buffoonery.[4,7] He fabricated ridiculous names, often symbols of the characters depicted. His later works turned satiric and were concerned with social problems. Hospital scenes and physicians figured prominently in his stories. His perceptiveness was acute, but his medical training probably honed to a keenness this talent for recognizing moral frailties, banalities, stupidity, and cupidity of his fellowmen.

His work does not reflect scorn, because he viewed human nature with a charitable eye, the mark of a compassionate physician. Unlike Tolstoy and Dostoevsky, Chekhov had a sense of humor, and through the pages "satire, sadness, gaiety and grief go hand in hand . . ."[7] Like a true realist he was able to see all sides of life, an ability he recognized in himself, and this may have been why he regarded psychiatry as appealing.

Of his many short stories, *Ward 6* interests me as a physician. This chilling portrayal of social conditions in Russia during the 19th century reveals the unspeakable deprivation, inhumanity, cruelty, and degradation of the peasantry. The tale of this mental hospital with its filth, uriniferous odors, bathtubs filled with vegetables, and brutal and dishonest ward attendants has been called a microcosm representing the social conditions existing in Russia 70 years ago.

The influence of his training as a physician is apparent in Chekhov's story *Typhoid Fever* which is an excellent clinical sketch. In *The Dual* two types of physicians are portrayed, one, an army surgeon, is appealing in his service to others but the second is more a usurer than a clinician. In *Three Years,* a young woman is operated on for cancer which later recurs. *Ionitch* depicts a rural practitioner who is rejected in marriage but builds a large practice and later rejects the same woman when she speaks of matrimony. In *Uncle Vanya,* Doctor Astrov works night and day and regards life as a nuisance, stupid and dirty, but endangers himself when he visits a village where typhus is endemic.

Chekhov on Medicine

On the occasion of his 25th anniversary as a writer, Chekhov wrote in a medical journal: "Medicine is my occupation, and to such a degree, in fact, that some time during the year I perform more forensic medical dissections than I once completed in two or three years."[7]

On another occasion he wrote: "I have no doubt that the study of the medical sciences has had an important influence on my literary work; they have considerably widened the range of my observations, and enriched me with knowledge, the true value of which to me, as a writer, can be understood only by one who is himself a doctor."[8]

Chekhov stated; "My family name and my crest I have given to medicine which I shall not desert for the rest of my life."[2] To Bilibin he said; "Sooner or later I shall part with literature."[2]

The Nature of the Man

Doctor Chekhov appears as an appealing man and the fact that he chose medicine as a vocation indicated his interest in human welfare and perhaps his need for human contact. He did not retreat from the demands of his patients because of aversion to human suffering but rather because of his restlessness and creative spirit which demanded other means for fulfillment.

He cherished friends and at times he entertained in a fashion too extravagant for his means. He was not immoderate in drink, had no publicized passionate or elicit romances, and was not obsessed with wealth despite his impoverished early years.

He was stubborn, sometimes obstinate, but showed none of the irascibility or temper tantrums of Dostoevsky. Impatient and demanding of himself, he seldom mistreated his friends, nor is there any evidence that he was anything but a considerate physician to his patients. He dealt with servants, waiters, porters, and simple folk with gentleness.

Kuprin,[9] a Russian author, stated that Chekhov had "incomparable spiritual firmness and beauty . . . the most beautiful, refined, and spiritual face I have ever seen in my life . . ."

His sister was devoted to him and proved to be a wise and efficient manager of his estate. She felt jealous and displaced when Anton married Olga Knipper but this did not affect the friendship between Anna and Olga.

Thomas Mann[10] noted that Anton was irritated by the imperial and prophetic airs of Tolstoy. Chekhov wrote: "To devil with the philosophy of the mighty ones of this world! All sages are as despotic as generals and as rude as generals, convinced as they are of impunity."[10] This outburst was occasioned by Tolstoy's denunciation of physicians as "useless scoundrels."

Mann[10] maintained that Chekhov suffered from honorable sleeplessness, feeling responsible for human fate. "What are we to do?" was a question often uttered by Chekhov. To Chekhov, Dostoevsky's work was "good but immodest and pretentious." From these reflections we can imagine that Chekhov suffered much from an enormity and depth of conscience.

The entire cast of *The Cherry Orchard* came from Moscow to perform for him at Yalta,[8] surely a magnificent display of love and respect. This play and Stanislavsky's genius combined to make the world aware of the Moscow Art Theatre.

Solzhenitsyn* is the most popular Soviet author outside the USSR and it is interesting to compare him with Chekhov for his portrayal of conditions within the Soviet Union. *Cancer Ward* has great similarity to *Ward 6* in depicting the suffering, humiliation, and despair of patients in a ward for those with malignant tumors. Because of the criticism implied of the Soviet system and because his works have been published in the West, Solzhenitsyn is not recognized but is a non-person in the USSR.

Although he never wrote a novel, Chekhov is ranked with Pushkin by Pasternak for "his child-like Russian quality and shy reticence." He deserves acclaim from physicians for his dedication to medicine. It is true that he spent little time in the practice of medicine but spent much time with patients when he was not writing. He was dedicated to the needs, physical and emotional, of his fellow man.

*Recently awarded the Nobel Prize in literature.

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Book Reviews

OPERATIVE TREATMENT OF BONE TUMORS. 3rd International Symposium, January 24th-26th, 1969 in Basle, Switzerland. Edited by George Chapchal. Stuttgart, Georg Thieme, and New York, Intercontinental Medical Book Corporation, 182 pp, 1970.

This is a collection of the papers presented at the Orthopaedic Department of the University of Basle. The participants are to be congratulated on setting aside time to discuss this most important aspect of orthopedics. Such an effort has not been evident on the North American continent in recent years.

In the section on pathology and diagnosis, a most interesting study was one by F. J. Makai and A. Belan emphasizing the prevalence of the spread of primary bone tumors by lymphatic routes. One table suggests that positive lymphograms are associated with a shorter survival time in patients with malignant bone tumors.

The remainder of the text is devoted to results of treatment, case presentations, and methods for excision of tumors and reconstruction of the resulting defects. The methods are varied and reveal courage and surgical ingenuity. One participant reported his experience with excision of the distal femur or proximal tibia and replacement with homotransplants preserved at —30 C or in polymer briquettes. Another investigator described his results after resecting the tumor-containing bone, irradiating the bone with Co^{60}, and then re-implanting the bone segment.

The symposium is interesting and is directed to the orthopedist whose main interest is orthopedic oncology.

Patrick J. Kelly, M.D.
Rochester, Minnesota

RESPIRATORY PHYSIOLOGY. Second Edition. By N. B. Slonim and L. H. Hamilton, C. V. Mosby. St. Louis. 1971. 230 pp. $10.75.

CARDIOVASCULAR PHYSIOLOGY. Second Edition. By R. M. Berne and M. N. Levy. C. V. Mosby. St. Louis. 1972. 265 pp. $9.25.

These two slim segments of clinical physiology are updated versions of first editions that appeared in 1967. *Respiratory Physiology* is written for the non-physiologist especially for the clinician, frankly, I think, for graduate students about to be examined in the field. It is a useful primer of respiration for all clinicians. One should not quarrel with the physiology but one might question the almost clinical statement that is made in the book that healthy trained subjects never experience true dyspnea. I have had many patients describe their cardiac dyspnea as shortness of breath just like the sensation after running only it occurs with much less exertion. *Cardiovascular Physiology* has a front cover illustration of the left ventricular pressure curve and one lead of the electrocardiogram. In a sense the whole book is an elaboration of the implications of these two curves. The great changes wrought in the past five years in cardiology are manifested in the majority of references which are in work, published since 1967. Both books merit perusal by all students whether or not they are about to be examined for degree or diploma.

Reuben Berman, M.D.
Minneapolis, Minnesota

TEXTBOOK FOR THE ORTHOPAEDIC ASSISTANT —F. R. Schneider, C. V. Mosby Co., Price: $10.75.

This textbook is clearly written and well illustrated and indexed. The basic aspects of musculoskeletal development and physiology are adequately described, and the terminology used to describe fractures and other musculoskeletal conditions is well covered. The "whiplash" injury to the neck is a lay term, however, and its use should be discouraged by those involved in treating cervical spine injuries. Plaster and traction techniques are superbly explained and illustrated and the fundamentals of orthopedic history taking and physical examination described. The importance of close observation of patients in Bryant's traction is stressed. Rewrapping of both legs daily in an attempt to prevent serious vascular complications should also be emphasized.

Although written for the orthopedic assistant, this book offers much information that is useful to the medical student, general practitioner treating orthopedic problems, and the orthopedic resident early in his training.

Lee C. Detenbeck, M.D.
Rochester, Minnesota

EMPHYSEMA by Fred A. Obley, M.D. published by Beacon Press, Boston. Price: $7.50, 116 pages.

This is an excellent book for patients suffering from emphysema and could be well recommended by the physician who has numerous occasions to treat this disease.

Carl O. Rice, M.D.
Minneapolis, Minneosta

SYNOPSIS OF DERMATOLOGY by Wm. D. Stewart, M.D.; Julius L. Danto, M.D.; and Stuart Maddin, M.D. October 1970. The C. V. Mosley Company, $13.85.

This second edition of Synopsis of Dermatology is an excellent book for both students and practitioners. The text is divided into four sections. The first deals with the development, structure, and function of the skin. Second, the office practice of dermatology is discussed. Regional diagnosis is next covered, while the final section describes individual diseases.

Discussion of the various dermatologic conditions are by necessity short in a book of this length (pp 445). However, the descriptions are adequate and well written. In addition, many of the newer concepts in both diagnosis and treatment of dermatologic disease are covered. The authors, for each disease, include a clinical description, differential diagnosis, and treatment. It should be noted that this book is well illustrated with many color plates, most of which are of excellent quality. This book should be of value for those interested in clinical dermatology.

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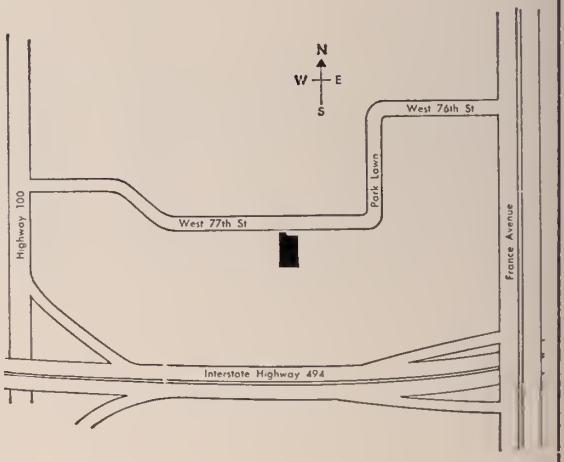
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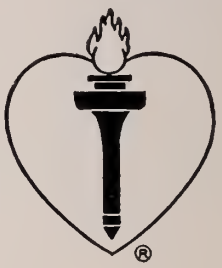
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Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
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President's Letter



Nothingness?

YOU STAND, with some other physicians, as your name and state are intoned from off stage and for approximately four blinding seconds you are spotlighted. Thus each state and territorial medical society is officially recognized at the American Medical Association's President's Inaugural ceremony.

Representing the Minnesota State Medical Association on that occasion was similar to an experience of nothingness in miniature. Visually isolated from all around you, auditory sensation dulled by the sameness of the repetitious calling of the roll, no tactile awareness of others. Hello! Is anyone out there. The spotlight shifts to the next and then the next until all are so honored. Your eyes accommodate applause marks the cessation of the droning roll call, you are jostled by your neighbors when sitting down on the crowded platform. You are once again with humanity and it's a welcome relief.

Isolation is unpleasant for most of us. I, for one, am uncomfortable when insulated from my colleagues. My first two letters to you dealt with the humanness of medicine as a profession in our contacts with each other as well as with our patients, and about changes occurring in our State Association and the American Medical Association. It has been rewarding and instructive to receive some response concerning those subjects. Visual, auditory and tactile insulation from Minnesota physicians is something your president is determined to avoid.

Hello! Is there anyone else out there?

George B. Fratus

President
Minnesota State Medical Association

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William Mahoney

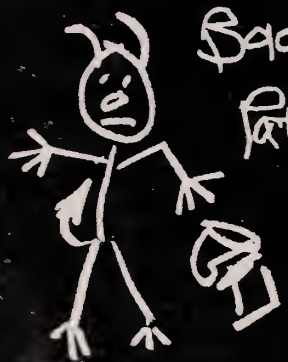


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Suzie McGuire



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—George Sarton, from "The History of Medicine Versus the History of Art"

Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

13.3%
Yes, it would be useful.

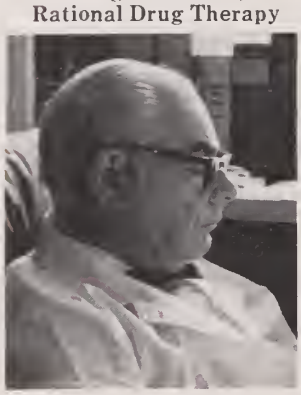
86.7%
No, it would not be useful.

Dialogue

Would it be useful in clinical practice to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

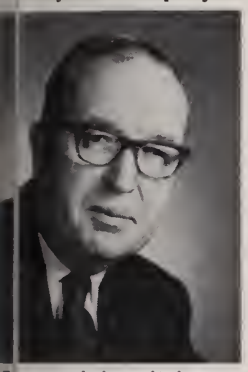
I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy in practice can rea determined.

The Bureau of Dru suggested the packa sert as a possible me communicating inform on relative efficacy of to the physician. I fin objectionable, since not believe the phy should have to rely o source for final sci truth. There is also a tical objection: Sinc physicians actually pense drugs, they s see the package inse any event, I would tain that the phys should know what dr wants and why witho pending on the gover or the manufacturer him.

Undoubtedly, physi are swamped by exc numbers of drugs in therapeutic categories I am well aware that drugs within such te gories could be elimi without any loss, or e haps even some prof the practice of medi But, in my opinion, ne the FDA nor any o single group has the e tise and the wisdom n sary to determine th "drug of choice" i al areas of medical practi

Maker of Medicine

n·th G. Kohlstaedt, M.D.,
Vice President,
Medical Research,
E Lilly and Company



I my opinion, it is not e nction of any governe or private regulatory e y to designate a "drug c ice." This determina- ı hould be made by the ıcian after he has re- i l full information on e roperties of a drug. n en it will be based on s xperience with this u and his knowledge of e ndividual patient who s king treatment.

I n evaluation of com- ar ive efficacy were to be a , particularly by gov- n ent, at the time a new u is being approved for a eting, it would be a r disservice to medi- n nd thus to the patient t consumer. For exam- e hen a new therapeu- t ent is introduced, on e asis of limited knowl- g it may be considered more potent, more f tive, or safer than r ucts already on the a et. Conceivably, at i time the new drug ı be labeled "the drug ıoice." But as addi- ı l clinical experience is c nulated, new evidence a become available. a , it may be apparent that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audiovisual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use — information that the pharmaceutical manufacturers must begin to provide if government regulation of *"drugs of choice"* is to be avoided.

Opinion & Dialogue

What is your opinion, doctor?
Send us your comments on the above issue.

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RONALD OLIN, M.D. and MARLIN H. POINDEXTER, M.D.

FAMILIAL MULTIPLE ENDOCRINE deficiencies are being reported with increasing frequency. Because they can be associated with such diseases as superficial moniliasis, pernicious anemia, Hashimoto's thyroiditis and steatorrhoea, a great number of clinical presentations are possible. The demonstration of circulation serum auto-antibodies to endocrine glands, intrinsic factor and parietal cells of the stomach suggests an inherited abnormality in the immunologic mechanism accounting for all these findings.

This report describes two sisters with idiopathic hypoparathyroidism and chronic mucocutaneous moniliasis, one of whom also had "adult-form" pernicious anemia and Addison's disease and the other serum adrenal auto-antibodies. Their mother and a younger sister have auto-antibodies to gastric mucosa. Their father, a brother and another sister are normal.

Pernicious anemia of the "adult-form" is extremely uncommon before age 20; our patient is the sixth reported case documented by modern methods. The combination of idiopathic hypoparathyroidism, superficial moniliasis, pernicious anemia and Addison's disease in a patient has been described only once previously.[1]

Report of a Family

Parents

Both are of Scandinavian ancestry, unrelated and are presently in good health. There is no other known family history of endocrine deficiency or pernicious anemia. In 1964, both had normal Schilling tests. The mother's serum reacted to gastric mucosa but not to thyroid microsomes or adrenal cortex (Table 1).

Jerome

Born 2-24-50. He had normal growth and development. As of August, 1971, he had no signs of endocrine deficiency, pernicious anemia or superficial moniliasis.

Linda

Born 10-30-51. She had Thrush in infancy. In January, 1958, she developed parasthesias of the hands and feet and carpopedal spasm. A positive Chvostek's sign was noted. The serum calcium was 8.6 mg.% and phosphorus 6.6 mg.%. These became normal when vitamin D and calcium gluconate were started. In January, 1959, hypoplastic teeth with deficiency of enamel were noted. In January, 1963, she became pale and weak. Her hemoglobin was 5.2 gm.%, hematocrit 16 vols.%, leukocyte count 6,000 per cmm. with a normal differential and the platelet count 80,000 per cmm. She had a histamine-fast achlorhydria. Her bone marrow examination showed a megaloblastic erythrocytosis with large metamyelocytes. A Schilling test revealed 1.8% excretion before and 18.1% excretion of labeled Vitamin B_{12} after intrinsic factor. Vitamin B_{12} injections were started and the hemoglobin soon rose to normal. In 1964, her left thumbnail showed moniliasis. The moniliasis was successfully treated with Fungizone lotion.

Additional studies at that time revealed a low serum iron and high latent iron binding capacity, a normal gastric mucosal biopsy except for the absence of parietal cells, normal thyroid function and no evidence of malabsorption. Serum studies revealed the presence of auto-antibodies to gastric mucosa and adrenal cortex. The parents were

Table 1
The Incidence of Antibodies in the Serum:

	Thyroid Microsomes	Adrenal Cortex	Gastric Mucosa (Parietal Cells)
Mother	—	—	+
Linda	—	+	+
Veronica	—	+	—
Cynthia	—	—	+
Cheryl	—	—	—

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advised to watch for Addison's disease.

In November, 1968, an eruption caused by T. gypsum developed on both elbows. The eruption cleared up with Griseofulvin therapy. Medications at this time were calcium gluconate two tablespoons daily, vitamin D 100,000 units daily and vitamin B_{12} 100 micrograms intramuscularly monthly.

She was seen again on January 4, 1971, with a four month illness consisting of weakness and weight loss of 50 lbs. (235 to 185 lbs.). She was hypotensive, and her skin had a brownish tinge. Plasma cortisols were 1 microgram at 8:00 a.m. and 3:00 p.m., and 24 hour urine for 17-Ketosteroids and 17-ketogenic steroids was 0.9 mg. and 0.6 mg., respectively. Serum sodium, chloride and blood sugar were moderately reduced and serum potassium was normal. She improved with intravenous saline infusions and parenteral steroids and was dismissed from hospital one week later on Cortisone acetate 10 mg. thrice daily and Florinef 0.1 mg. once daily. She has been well on follow-up examinations, her latest in August, 1971.

Veronica

Born 5-11-53. Frequent upper respiratory infections were present in childhood. In August, 1957, a convulsion occurred during a respiratory infection. Chvostek's sign was positive, carpopedal spasm was present. Serum calcium was 6.2 mg. % and phosphorus 10.4 mg. %. The Elsworth-Howard test indicated hypoparathyroidism. Calcium gluconate and vitamin D were started with a good response.

In 1964, she was noted to have mycotic fingernails, thrush, bilateral semiptosis, and healed keratitis. Mycostatin oral suspension and Fungizone lotion were prescribed. Serum iron was low and the latent iron binding capacity high; thyroid function was normal; Schilling test and gastric mucosal biopsy were normal. There was no evidence of malabsorption. Her serum contained auto-antibodies to adrenal cortex but as of August, 1971, no signs of adrenocortical insufficiency had developed.

Cynthia

Born 12-16-54. As of August, 1971, she was healthy with no evidence of endocrine deficiency, pernicious anemia, or superficial moniliasis. In 1964, her serum contained auto-antibodies to gastric mucosa.

Cheryl

Born 4-11-57. As of August, 1971, she was healthy with no evidence of endocrine deficiency pernicious anemia or superficial moniliasis. I 1964 her serum was negative for auto-antibodie against thyroid microsomes, adrenal cortex an gastric mucosa.

Discussion

Idiopathic hypoparathyroidism is an uncommo condition usually manifesting in childhood. It i approximately twice as common in females tha males. Steinberg and Waldron in 1952[2] reviewe 52 cases from the literature including three sibling affected in the family described by Sutphin, et al. Seven of the 52 cases had mucocutaneous monili asis. The cause of idiopathic hypoparathyroidisr is unknown but an auto-immune mechanism i suspected because one-third or more cases hav circulating parathyroid auto-antibodies.[4] This as sumption is further supported by the frequen association of other diseases suspected as bein auto-immune in etiology; namely, Addison's dis ease, pernicious anemia and Hashimoto's thyroid itis. The frequency of auto-antibodies in the ser of patients with idiopathic hypoparathyroidism is[4]: parathyroid tissue 38%, adrenal cortex 11% (normal adrenal function), gastric parietal cell 16% (no overt pernicious anemia) and thyroi microsomes 13% (normal thyroid function). On or more endocrine deficiency diseases may co-exis in the same patient or may alternate in member of the same family.

Mucocutaneous moniliasis occurs commonly i patients with idiopathic hypoparathyroidism an Addison's disease. Blizzard and Gibbs in 1968 reviewed 44 patients (29 females and 15 males over age one year who had mucocutaneous mon iliasis. Thirty-one patients had some associate disease (Table 2). There were five pairs of siblings Only seven of the 31 cases had no antibodie detectable in any tests to endocrine glands o

Table 2
Associated Diseases With Moniliasis

	Female (24)	Male (7)	Total (31
Idiopathic hypoparathyroidism	21	5	26
Idiopathic Addison's disease	9	5	14
Pernicious anemia	7	0	7
Hashimoto's thyroiditis or spontaneous myxedema	2	1	3
Alopecia totalis or universalis	4	2	6
Juvenile cirrhosis	3	0	6
Ovarian failure	3	0	3
Splenic agenesis	1	0	1

stomach. Moniliasis often improved when hypocalcemia was corrected. No evidence was found that moniliasis was either the cause or the result of the associated disease processes.

Pernicious anemia before age 20 with the absence of intrinsic factor has been reported in only 26 patients.[6] These can be subdivided into two groups: (1) 21 cases in which gastric acids and gastric mucosa histology were normal and (2) five cases in which there was a histamine-fast achlorhydria and gastric mucosal atrophy. In the latter group, antibodies to gastric parietal cells or intrinsic factor were detected in the serum of four cases, associated endocrine deficiencies were present and the anemia developed between the ages of 10 to 18 years. The etiology may represent an acquired atrophy of the gastric mucosa such as has been postulated in adults with pernicious anemia.

In contrast, the age of onset in the first group was before two and a half years in the majority. The etiology in this group may be a metabolic error, perhaps a selective biochemical abnormality of gastric parietal cells with failure of intrinsic factor secretion. There were five pairs of affected siblings among the 26 cases. A study of parents of two of these families suggested that the disorder may result from the homozygous inheritance of a gene responsible for the development of pernicious anemia in adult heterozygotes.

The frequency of auto-antibodies in the sera of a large group of patients with pernicious anemia is:[7,8] intrinsic factor (blocking only) 19%, intrinsic factor (blocking and precipitating) 34%, gastric parietal cells (stomach mucosa) 75% and thyroid tissue (cytoplasm) 37%.

Five cases of co-existent idiopathic hypoparathyroidism and pernicious anemia have been reported.[9-13] Three[9,10,13] of the five had no other associated diseases and auto-antibodies were not sought in their sera. In the fourth case, reported by Morse, et. al.,[11] the patient also manifested superficial moniliasis and an incomplete form of cystic fibrosis of the pancreas. Circulating auto-antibodies against intrinsic factor were detected but not against parathyroid tissue. Four of this patient's ten siblings had idiopathic hypoparathyroidism and elevated levels of sweat sodium and chloride, two had Addison's disease and one may have had pernicious anemia.

The onset of pernicious anemia in young patients has always followed the onset of idiopathic hypoparathyroidism by five to ten years. Comin, et al. in 1969[14] reported the first case of pernicious anemia co-existent with idiopathic hypoparathyroidism in an adult woman, age 46. Pernicious anemia was diagnosed at age 40 and idiopathic hypoparathyroidism at age 43, in contradistinction to the order of onset of the two diseases in childhood. The demonstration of circulating auto-antibodies to thyroid microsomes, adrenal cortex and intrinsic factor indicated a similarity between the childhood and adult syndromes.

Familial Addison's disease is also an uncommon entity. In 1959, Meakin, et al.,[15] reviewed the literature and found five reports documented by steroid studies or autopsy findings[16-20] and reported another in two brothers. Since that time, four additional reports fulfilling their criteria have been published.[21-24] The association of idiopathic hypoparathyroidism, superficial moniliasis and Addison's disease is even rarer, only eight patients being reported in the literature.[1,3,25-29] Hung, et al.,[1] and Quinto, et al.,[12] described a family in which Addison's disease was present in three siblings, one of whom also had the first reported combination of idiopathic hypoparathyroidism, superficial moniliasis and pernicious anemia. Auto-antibodies were detected to adrenal cortex and intrinsic factor but not against parietal cells or thyroid microsomes. Their patient developed idiopathic hypoparathyroidism at age four (ours age six), Addison's disease at age eight (ours age 19) and pernicious anemia at age 10 (ours age 11).

The frequent association of Hashimoto's thyroiditis and Addison's disease has long been recognized.[30] A case of triple deficiency of parathyroid, adrenal and thyroid function was presented by Carter, et al., in 1959.[31] In 1964, Kenny and Holliday[32] presented two sisters with idiopathic hypoparathyroidism and superficial moniliasis, one of whom also had Addison's disease and Hashimoto's thyroiditis (thyroid and adrenal antibodies present), a combination previously undocumented, and the other had no other diseases (no thyroid or adrenal antibodies present).

Primary ovarian failure has been described in Addison's disease. Irvine, et al., in 1968[33] carried out a serologic and histologic investigation to determine if antibodies reactive to ovarian constituents were a feature of Addison's disease. Antibodies were found in five of 77 patients with

Addison's disease all of whom had had either a complete failure of menstruation or an early menopause. There was serologic evidence that some cases of premature ovarian failure may have an auto-immune basis.

Summary

The importance of evaluating multiple endocrine function in children or adults with an idiopathic endocrine failure is demonstrated in a family. An important point is that circulating auto-antibodies may signal occult disease which can become manifest at some future time.

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Medical Names and Initials

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THE EPONYM UNDOUBTEDLY began to be used in medicine long before written records were kept. Numerous parts of the human body had eponymical designations, and many diseases still bear the name of distinguished clinicians. A long list of clinical signs and symptoms are named after investigators who first described or popularized them, and various tests and procedures are known only by the name of the originator.

The eponym still serves as a useful and convenient form of medical shorthand, as illustrated by terms such as Fallot's tetralogy, Benedict's sugar reagent, and Trousseau's sign. Sometimes too it is a means of acknowledging notable achievements cogently illustrated by such terms as the Mendelian laws of heredity, and Pasteurization. As a rule, eponyms are short-lived and rarely a vehicle for conferring lasting fame. A good memory for eponyms is hardly ever evidence of medical erudition, and slavish adherence to outmoded eponyms may block progress.

Initials, likewise, are useful and convenient, but they can result in confusion. P.T. is the commonly accepted abbreviation for the one-stage prothrombin time but the test is not specific for prothrombin, measuring several clotting factors. The abbreviation T.T. in hematology may stand for the thrombin time, thromboplastin time, thrombo test, or the tourniquet test. Such initials may become very confusing.

When initials are based on uncertain or inaccurate terms, misinterpretations of even such well known expressions as I.T.P. may occur. While I.T.P. is tacitly accepted to mean idiopathic thrombocytopenic purpura, it is doubtful whether idiopathic, which means of unknown origin, is always correct since the cause may be known. Much greater clarity could often be achieved if the meaning of "I" were changed from idiopathic to immune.

Eponymization in Hematology

Eponymization in the bleeding states began after Werlhof gave the imposing name of morbus maculosis haemorrhagicus to purpura, a term soon replaced by Werlhof's disease. Nearly a century later, Schönlein recognized another type of purpura which he called peliosis rheumatica because it was accompanied by joint symptoms. Soon, it was given the name of Schönlein's purpura and when Henoch described a purpura associated with gastrointestinal bleeding, it too, soon bore his name and, when it was later found that the two types of purpura were different manifestations of the same disease, the names of Schönlein and Henoch were linked. When it was found that the platelet count in Werlhof's purpura was reduced, while it was normal in number in the Schönlein-Henoch purpura, the differential diagnosis of the two types was established. Though much of the work resulted from the creative contributions of the French hematologist Hayem, he is now known to many hematologists only because his name is attached to the useful reagent—Hayem's solution.

Von Willebrand's Disease

The disease now commonly designated as von Willebrand's disease probably represents hematological nomenclature at its worst. The blame for this can be found in the irregular manner with which most medical knowledge has developed. As already pointed out, Werlhof's purpura was the first and the only clearly designated bleeding disease. In 1802 Otto described "a hemorrhagic disposition" with a characteristic hereditary pat-

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tern which led to the establishment of the condition as a distinct disease which 24 years later assumed the permanent name of hemophilia. In this entity, the clotting time was found to be prolonged. Thus, it was the first bleeding disease in which a laboratory test became useful for diagnosis. At the beginning of this century, only two bleeding states were generally recognized—purpura and hemophilia—and the common laboratory test was the clotting time which was crude and unstandardized. Gradually, this void was filled by the bleeding time of Duke in 1910, more careful standardization of the clotting time by Lee and White in 1913, and the introduction of the tourniquet test into America by Hess in 1914.

It was these three tests that substantiated the statement Hess made in 1916: "It is becoming increasingly evident that the group termed 'hemorrhagic diseases' includes a large number of abnormal conditions and that at the present time it is a fruitless task to attempt to unravel the various entities . . ." It was Minot and Lee, who, in 1920, began the unravelling of these states when they reported a family with familial recurrent epistaxes and a prolonged bleeding time but a normal clotting time and platelet count. Minot was aware that epistaxis was just one finding in this systemtic disorder which, in 1928, he described succinctly: "There exists a chronic familial hemorrhagic condition characterized by a prolonged bleeding time in the absence of a decrease of blood platelets and a delayed coagulation time of the blood. Multiple ecchymoses and recurrent epistaxis are characteristic symptoms. Pathologic blood loss and abnormal bleeding may be present at one time and not at another, but their occurrence is not necessarily synchronous. This hemorrhagic condition appears in infancy and may extend into adult life, but then its severity tends to decrease and the condition may disappear as the patient grows older."

Minot did not give the disease a specific name. During this period, von Willebrand studied a family with a similar bleeding state living on the Åland Islands in the Baltic Sea. His first report in 1926 was in a Finnish medical journal and it was therefore not until 1931 when he reported in German that his findings became readily available. In his patients it too was the prolonged bleeding time that was the outstanding feature of the disorder. Von Willebrand called the disease hereditary pseudohemophilia but after he and Jürgens (R.) presented what they considered as evidence of defective platelets, the condition in the European medical literature began to be commonly called the von Willebrand-Jürgens constitutional thrombopathy and this has now been simplified to von Willebrand's disease.

Rendu-Osler Disease

The clinical condition reported by Rendu in 1896 in which he observed hereditary recurrent epistaxes with characteristic skin and mucous membrane lesions has been an especially eponymophilic disease entity. Osler's name supplied valuable prestige but to it have been added the names of Sutton, Parkes-Weber, Goldstein, and others. Hanes offered the valuable suggestion that the disorder be named hereditary hemorrhagic telangiectasia. This helped to simplify the nomenclature and also to characterize better the nature of the disease, which none of the eponyms had done. What is apt to be overlooked is that telangiectasia is a purpura and that bleeding is not merely from the more spectacular telangiectatic lesions but also from those of minor importance. In many patients with the trait, both the tourniquet test and the bleeding time are abnormal, though the platelets are normal in number and quality.

Glanzmann's Purpura

In 1918 Glanzmann described a new hereditary diathesis appearing in both sexes in which bleeding was of the purpuric type—oozing from mucous membrane, and hemorrhaging into the skin. The bleeding time, the clotting time and the platelet count were normal but clot retraction was delayed or absent. Such a combination of laboratory findings has never since been reported, but I have had the opportunity to study a purpuric state simulating in many aspects, the findings of Glanzmann. The patient has a severe purpuric condition at birth and, for over two years, she completely lacked clot retraction despite a normal platelet count. She has, however, a very long bleeding time and a very poor prothrombin consumption. Clot retraction is gradually improving but not the bleeding time nor the prothrombin consumption time.

At the time that Glanzmann reported his cases, precise and highly standardized tests for platelet function were not available but, despite this han-

icap, he made the important contribution by mphasizing that the role of platelets in hemostasis epends not only on their number but also on heir quality. His term "thrombasthenia" is still alid and his speculation that clot retraction was ue to an enzyme, retractozyme, while not strictly orrect, was the forerunner of the retractile pro- ein thrombosthenin.

Just as von Willebrand's disease is basically haracterized by a prolonged bleeding time, so Glanzmann's disease has as its key defect, faulty lot retraction. But defective clot retraction, ex- ept in acquired thrombocytopenic purpura, is xceedingly rare. Far more important in heredi- ary platelet dysfunction is the lack of a specific latelet clotting factor which is usually designated s platelet factor 3 (PF_3). The clotting factor in latelets is readily diagnosed and quantitatively neasured by the prothrombin consumption test.

Hereditary Non-Thrombocytopenic Purpura

These hereditary states chiefly known by their eponymic designation can be grouped under the general term of hereditary non-thrombocytopenic purpura. In all, the clotting time is normal and the platelets are, at the most, only moderately reduced. All have in common that the bleeding time may be entirely normal but often prolonged and, in many instances, significantly. Likewise, the tourniquet test shows the same variations. The prothrombin time is normal or only slightly prolonged while the prothrombin consumption test may also be normal. When abnormal, the latter test becomes a critical factor in the differential diagnosis. Inconsistencies in platelet adherence and aggregation have also been recorded.

The condition is essentially purpuric. Epistaxis is the most common form of bleeding, especially in childhood, and easy bruising is almost equally as common. Menorrhagia is frequent but menses may be entirely normal. Gastrointestinal bleeding, while usually infrequent and mild in youth, may be most troublesome and alarming in old age. Paradoxically, a minor surgical operation such as a tonsillectomy or tooth extraction may give rise to serious bleeding, whereas the same patient may undergo a major abdominal operation with impunity. Traumatic bleeding seen in hemophilia, such as hemarthrosis, deep intramuscular bleeding and hematuria, is conspicuous by its absence. This clinical state has befuddled the physician to whom such patients first turn for help.

In attempting to understand the state of the hereditary, nonthrombocytopenic purpuras, it must be recognized that the eponyms have outlived their usefulness. For instance, the Rendu-Osler disease as a distinct clinical entity is probably very rare. It is a common hereditary trait that only gives clinical manifestations when associated with another hemostatic defect and subjected to provocative agents of which aspirin and, perhaps, alcohol are the most common. Most of the states designated as Glanzmann's disease are thrombopathies in which thrombasthenia (lack of clot retraction) is a subordinated facet of platelet dysfunction. Von Willebrand's disease is a conglomerate of inherited defects, many of which would have remained dormant had it not been for the introduction of aspirin into therapy. This drug not only called attention to the defect by prolonging the bleeding time but also by accentuating the bleeding tendency.

It is certain that in a segregated population such as that of the Åland Islands, a trait such as telangiectasia, which is transmitted as an autosomal dominant, is likely to be as common as the still undefined von Willebrand trait. Then, too, the aspirin intolerance as measured by the aspirin tolerance test appears to be transmitted as an autosomal dominant. This is also true of one type of hereditary thrombopathy which is diagnosable by the prothrombin consumption test.

Telangiectasia is now known to exist in one family of the Åland pedigrees,[1] and also in an Icelandic family reported as von Willebrand's disease.[2] Edson[3] has seen one case in which telangiectasia co-exists in a patient whom he had diagnosed as von Willebrand's disease.

Numerous cases formerly diagnosed as von Willebrand's disease have later proved to be combinations of telangiectasia and aspirin intolerance, telangiectasia and hereditary thrombopathy, and other combinations of mild hemostatic defects. The pitfalls in diagnosis have been that: (1) basic laboratory tests such as the bleeding time, and the tourniquet test, the prothrombin consumption time are often not carried out nor interpreted properly. (2) the patient's history is often incomplete and the importance of spontaneous epistaxis in childhood overlooked, and (3) the telangiectatic lesions are missed.

Rather than cling to eponyms that have out-

lived their usefulness, names such as Rendu, Osler, Glanzmann, Minot, von Willebrand can be consigned to the history of medicine and the purpuric bleeding states redesignated on the basis of more exact diagnostic criteria. Telangiectasia is perhaps the most specific to diagnose. In the adult the lesions are most common on the back, arms, chest and face but are often absent in mucous membranes. In many patients, the tourniquet test is usually strongly positive. In children the typical lesions may not be present but only appear later in life.

All purpuric cases should have in addition to an accurate medical history and a physical examination, standardized bleeding, tourniquet, prothrombin, prothrombin consumption, and aspirin tolerance tests performed. It should also be borne in mind that most patients with purpuric bleeding have dual or multiple defects.

Disseminated Intravascular Clotting (DIC)

Intravascular clotting has been recognized since the time of Harvey and it is difficult to state exactly what "D" in the combination of DIC really means. DIC, furthermore, has been closely associated with another pathological process—consumption-coagulopathy. In 1935 my associates and I[4] carried out what was perhaps the first experimental consumption-coagulopathy. We described it as follows: "A freshly prepared and filtered saline extract of rabbit brain (20 cc.) was injected intravenously into a dog. A severe reaction occurred immediately, respirations became shallow, and a nystagmus developed. The fibrinogen which was 0.44% before the injection dropped to 0.09 in five minutes and to a mere trace 30 minutes after the injection. The dog was killed one hour later and autopsied. No definite intravascular clotting could be found, but there was a relatively small pulmonary infarct and also a small mesenteric infarct."

The first clinical report of consumption-coagulopathy was made in 1936 when Dieckmann[5] associated the obstetrical bleeding state characterized by lack of fibrinogen in the blood with premature separation of the placenta. It is now well established that both premature separation of the placenta and uterine retention of a dead fetus result in bleeding and that in this state several clotting factors in the blood are significantly diminished. Another condition in which a similar type of consumption-coagulopathy occurs is cavernous hemangiomas. In both the obstetrical states and in giant hemangioma a continuous escape of either preformed thromboplastin or thrombin into the bloodstream takes place at such a slow rate that massive thrombosis does not occur but the fibrils of fibrin and platelet aggregates are continuously filtered off in the capillary network. Such a process can also be produced by injecting a dilute solution of thrombin at a very slow steady rate directly into the bloodstream.[6] Under these circumstances, no massive thrombosis is produced but the circulating fibrinogen is slowly changed to fibrin and removed from the bloodstream. The platelets decrease in number and in quality. The prothrombin time becomes prolonged mainly because of a decrease of factor V and the prothrombin consumption time shortened because the consumption of prothrombin is blocked, first, by platelets reduced both in number and quality and, also, by decreased factor VIII. Eventually, fibrinolysin activity also becomes a dominant feature since profibrinolysin or plasminogen becomes activated and escapes into the bloodstream.

In such clinical or experimental states the complete picture of consumption-coagulopathy is produced. The disappearance of fibrinogen and the marked drop in the platelet count are easiest to detect but the diminution of factor V and VIII are equally striking. Prothrombin is reduced less and factors VII, IX and X are little affected. Crucial is the resulting lack of the platelet-containing factor usually called platelet factor 3. The states discussed are genuine intravascular clotting, not disseminated, since the source of the clotting agent, be it tissue thromboplastin or thrombin, is localized.

Many of the current papers dealing with DIC correspond to what was formerly designated I.T.P. Perhaps, the most common form of consumption coagulopathy is I.T.P. with its new meaning of "immune" thrombocytopenia. The fall in the platelet count may be gradual or precipitous but the replaced platelets are deficient in the clotting factor which is sensitively measured by the prothrombin consumption time test. Apparently, in the immune process, the platelets are aggregated and removed rapidly by filtration in the capillary beds. Too little reduction of the other clotting factors occurs to be measurable. DIC is therefore

not an accurate designation. According to the initial-system, DPA (disseminated platelet aggregation) would more closely describe the immune reaction.

No justification can be found for adopting DIC as an all-inclusive term. The extensive consumption-coagulopathy which is so prominent in placenta abruptio or giant hemangioma is entirely different from the various immune reactions grouped under the initialled designation. Both the basic etiology and the management are completely different. In some, heparin is the effective therapeutic agent and, in others, the corticosteroids. Sometimes, a fibrinolysin blocking agent such as epsilon-aminocaproic acid seems indicated. To base therapy on a blanket diagnosis of DIC can be disastrous.

The historical references can be found in the author's monographs: The Hemorrhagic Diseases and the Physiology of Hemostasis. Charles C. Thomas, Springfield, 1942. Hemorrhagic Diseases and Thrombosis. Lea & Febiger, Philadelphia, 1966. Bleeding Problems in Clinical Medicine. W. B. Saunders, Philadelphia, 1970.

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Tuberculosis

I had not seen him for ten days, and was appalled by the fearful alteration which the brief interval had wrought in him. His face wore a leaden hue; the eyes were utterly lustreless; and the emaciation was so extreme, that the skin had been broken through by the cheekbones. His expectoration was excessive. The pulse was barely perceptible. He retained, nevertheless, in a very remarkable manner, both his mental power and certain degree of physical strength. He spoke with distinctness—took some palliative medicines without aid—and, when I entered the room, was occupied in pencilling memoranda in a pocketbook. He was propped up in the bed by pillows. Doctors D..... and F..... were in attendance.

After pressing Valdemar's hand, I took these gentlemen aside, and obtained from them a minute account of the patient's condition. The left lung had been for eighteen months in a semi-osseous or cartilaginous state, and was, of course, entirely useless for all purposes of vitality. The right, in its upper portion, was also partially, if not thoroughly, ossified, while the lower region was merely a mass of purulent tubercles, running one into another. Several extensive perforations existed; and, at one point, permanent adhesion to the ribs had taken place . . . It was the opinion of both physicians that M. Valdemar would die about midnight on the morrow.*

*Edgar Allan Poe, "The Case of M. Valdemar" (short story, 1840).

Historic Hospitals

The Nuri Hospital, Damascus



Entrance to the Nuri Hospital. Damascus, Syria. Courtesy of the Smithsonian Institution, Freer Gallery of Art, Washington, D.C.

The most advanced hospitals of the medieval period were the Arab hospitals of the Eastern Caliphate. Outstanding among them was the Nuri Hospital at Damascus, pictured here. The hospital was founded by Sultan Nur al-Din Zengi in 1154 and its construction financed by the ransom collected for the release of a European king captured in the Crusades. The building surrounded a rectangular court with a pool in the center. Four open rooms on the main axis served as the consulting rooms of the physicians, while six other rooms provided wards for the patients. An annex was added in 1239, and running water installed in its various departments at that time.

The daily routine of the chief physician included daily hospital rounds, accompanied by his assistants and orderlies, examining patients and giving orders for their medication and care. After rounds he read and prepared lectures in the hospital library. For three hours each afternoon he sat with his physicians and students, teaching, discussing medical topics, and considering the difficult cases.

The hospital had a rich income for the time, provided by the sultan. Typical of the medieval Arab hospitals, there was no charge to the patients for their care. The food was said to be so good that malingerers occasionally entered just to partake of the hospitality.

Considerable prestige went with appointment to the medical staff of this institution which functioned as a public hospital for about seven centuries. The most distinguished advancement credited to the hospital, however, is not a strictly medical one, but pertains to the keeping of medical records. The register of patients kept by the administrator is probably the first of its kind in the history of hospitals. Beside each name the physician making his daily rounds recorded the orders for the day. This simple register was a prototype of the untold millions of hospital charts which today occupy complex medical records departments, some of which are larger than the entire Nuri Hospital.

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Intramuscular Neurolysis for Stroke

ESSAM A. AWAD, M.D., Ph. D.

It is estimated that half a million Americans suffer from cerebral vascular attacks each year, and that there are two million persons alive in the United States who have neurologic manifestations of stroke. This problem is also expected to become more prevalent because of the increase in longevity. Most of the stroke patients demonstrate varying degrees of functional impairment. Disability ranges from total incontinent dependency to almost complete self-sufficiency with residual difficulties in the use of the upper and lower extremities involved.

This communication concerns itself with a method proved helpful in restoration of useful function in the hemiplegic hand and in improving ambulation of the stroke victims.

Statement of the Problem

It is a widely known fact that the hemiplegic extremities manifest flexor spasticity, following the initial flaccid phase. This flexor spasticity and the associated paresis maintain the shoulder adducted and internally rotated, the elbow flexed, the forearm pronated, and the fingers and the wrist flexed. In the lower extremity, the hip and the knee are flexed and the ankle is plantar flexed. Spasticity involving the hand and the upper extremity often renders the hand useless for the patient. Spasticity of the plantar flexors of the foot interferes with the ability of the patient to walk; sometimes an ankle clonus develops whenever the gastrocnemius-soleus complex is stretched as the patient's forefoot touches the floor. In addition, the patient's heel tends to slip out of his shoe because of the spasticity and plantar flexion. The problem then is: (a) inability of the patient to grasp objects because of flexor spasticity of the finger and wrist muscles, (b) difficulty in ambulation due to spasticity and ankle clonus in the lower extremity.

Attempts to overcome spasticity through the use of drugs are far from satisfactory; many patients become drowsy and the spasticity is never completely abolished while the patient is fully conscious. Surgical procedures such as tenotomy or neuroectomy have been used. The technique to be described taxes the patient less heavily than any surgical procedure. In addition, it has the advantage of tailoring the degree of neurolysis to the individual muscle so that one can retain proper function and at the same time abolish undesirable spasticity.

Technique

Intramuscular neurolysis is a simple technique for control of spasticity in the stroke patient. This method applies to any skeletal muscle.[1] The following three steps are followed:

1. Localization of the motor point: This point is defined as the most irritable point of a given muscle, or the point on the skin at which an electrical stimulus of minimal amplitude and duration will result in a visible contraction of that muscle. The motor points of superficial muscles are easily defined. Motor point charts are available and serve as a good guide for the beginner.[2] Some muscles such as the gastrocnemius which have two heads, also have two motor points. The physiatrist, as well as the physical therapist, are both capable of performing this step. An electrical stimulator known as a "chronaximeter" is used for this purpose.

2. Insertion of needle electrode at the motor point and localization of the motor innervation band: An injection needle coated with an insulating substance except for its tip and connected to the output of the chronaximeter is inserted into the muscle at the motor point. The stimulus intensity is reduced to approximately one milliampere and its duration to 1/10th of a millisecond. This stimulus is repeated automatically at a rate of one or two per second. When the needle tip is in close contact with the motor

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See editorial, page 742.

nerve fibers, fascicles of the muscles will contract and relax rhythmically at the same rate as the electrical stimulus.

3. Phenol Injection: the injection of a trace (usually 0.1 c.c) of 5 percent phenol solution in water at this time will be followed by cessation of the contractions despite continued stimulation. The immediate effect of phenol makes it easy for the physician to determine the results instantaneously and to evaluate the patient's need for further blocks in the same muscle. The injection of one site results in denervation of only one fascicle in the muscle. If the spasticity is severe, one might have to block several points in one muscle until the desired effect is achieved, e.g., abolition of a clonus.

Results

Sixty-two intramuscular neurolysis procedures were performed on forty-one stroke patients. All patients were referred to us for control of hypertonus which interfered with hand function or with ambulation. Some patients underwent neurolysis of more than one muscle group during the first visit, e.g. plantar flexors of the foot and wrist and/or finger flexors. Several patients returned for a second and occasionally a third block. The duration of the effectiveness of a procedure was four to 14 months. It is extremely difficult to determine the duration of the effects because recurrence of spasticity is very gradual and takes place over a period of several weeks or months.

Twenty-nine patients underwent intramuscular neurolysis of the plantar flexor muscles of the foot in order to eliminate spasticity and clonus which caused shuffling of the forefoot during walking and apparent lengthening of the paretic lower extremity with resultant flexion at the knee and hip and circumduction of the leg.. These patients, also, had a tendency to trip over their foot during ambulation on a carpeted floor. Many were unable to keep their heels inside their shoes. Following this procedure the involuntary activity and ankle clonus were abolished in all cases leading to improvement of ambulation.

Twenty-two patients underwent intramuscular neurolysis of the wrist and/or the finger flexors of the paretic upper extremity. Prior to this procedure, the hand and wrist were held in severe flexor spasm (Figure 1). In three females, the neurolysis was performed in order to enable them to wear gloves or mittens during the winter. Ten patients were able to flex and extend the fingers of the paretic hand to the extent that they were able to hold the telephone receiver (Figure 2). This allowed them to use their other hand for writing. This is an important achievement in the vocational rehabilitation of the stroke victim. Twelve patients had good control of spasticity, but were unable to grasp objects with their paretic hand because of lack of finger extensor strength.

In five patients, intramuscular neurolysis was performed on the hip adductors of the paretic side. This was done at the same time the plantar flexors were blocked to control severe adduction of the lower extremity in order to improve the gait pattern.

Partial neurolysis of the hamstring muscles in five patients and of the quadriceps femoris in one patient was carried out to control spasticity and improve gait.



Fig. 1—Left hand of a patient who had a stroke for over two years, showing maximal voluntary extension prior to intramuscular neurolysis.



Fig. 2—Immediately following neurolysis of the finger flexors. the patient is now able to extend her fingers and to grasp objects.

Discussion

Intramuscular neurolysis is a process of chemical partial denervation. Reinnervation is to be anticipated with recurrence of hypertonicity. However, the relief lasts four to 14 months, depending on such factors as: (a) the extent of neurolysis performed; (b) the amount of phenol used; (c) the presence or absence of other factors which aggravate spasticity, such as urinary tract infections or skin ulcers; (d) recurrence of cerebrovascular accidents.

Because phenol solution results in aseptic coagulation necrosis of very small areas in the muscle, it leads to a certain amount of fibrosis, which seems beneficial as it interferes with the regeneration of the distal segment of the intramuscular nerve fibers. The cumulative effect of this incomplete reinnervation—following repetition of neurolysis—resulted in a permanent effect. In some patients there *was no* need for further neurolysis after repeating the procedure three or four times.

Phenol has passed the test of time and is accepted as a local blocking agent. It is free of local irritation and systemic toxicity, easily sterilized and available at low cost.

Since spasticity is a state of abnormally excessive involuntary contraction, due to increased activity of the myotatic reflex, it seems reasonable to control it by means of interruption of the pathway of this reflex. This is the effect of phenol on the intramuscular nerves.

Conclusion

Intramuscular neurolysis of spastic muscles is an excellent method to control hypertonicity in the stroke patient. In all cases, plantar flexors spasticity could be reduced and ankle clonus abolished. This enables the patient to walk with a better gait. In some cases, hand function could be substantially improved, to allow the patients to grasp objects and to wear gloves or mittens during the winter.

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Cover Photograph

"Mississippi Idyll"

Dr. Farrell Stiegler, Cover Editor of MINNESOTA MEDICINE, took this photo of the Medical School (Mayo Memorial) and the Showboat in January of 1971. He used a Linhoff 2¼ x 3¼ Camera with a 100 mm lens and Ektachrome Film.

Dr. Stiegler is a surgeon practicing in Minneapolis, and states that his reason for selecting this particular cover is to stimulate other physicians to submit more pictures of Minnesota to the Cover Editor of MINNESOTA MEDICINE.

A man doesn't live by bread alone. He needs buttering up once in a while.

Distinguished Teaching Award



(L-R) John W. Frost, M.D., chief of medicine at St. Paul-Ramsey and president of the Minnesota Medical Foundation; Wesley D. Anderson, D.V.M., Ph.D., recipient of the 1972 Distinguished Teaching Award jointly sponsored by the Minnesota State Medical Association and the Foundation, and George B. Martin, M.D., Thief River Falls, president of the State Association.

Wesley D. Anderson in the Anatomy Department has been chosen by medical students of the University of Minnesota to receive the 1972 Distinguished Teaching Award of the Minnesota State Medical Association and Minnesota Medical Foundation. The award of $1,000 is contributed by the Minnesota State Medical Association.

The 47-year-old associate professor of human anatomy was chosen for this honor by medical student poll. The award recognizes excellence in teaching medical students and also notes demonstrated concern for their welfare. Dr. Anderson is the 19th recipient in 11 years of the award program.

The award was presented in May by Dr. John W. Frost, president of the Minnesota Medical Foundation and Dr. George B. Martin, Thief River Falls, president of the Minnesota State Medical Association, co-sponsors.

Dr. Anderson received his D.V.M. degree from the University's School of Veterinary Medicine in 1951 and operated a veterinary practice in Rosemount, Minnesota, for 10 years. He left his practice in 1964 to join the faculty of the veterinary school. He also continued his graduate studies at the University Medical School and at the Mayo Graduate School in Rochester and received a Ph.D. in human anatomy in 1969. He joined the faculty of the Medical School shortly thereafter.

Dr. Anderson has engaged in many research projects, most of them dealing with tensile strength and blood flow in arterial systems of man and other animals.

Single, Combined and Sequential Use of Uracil Mustard and Prednisone

in the Treatment of Lymphoreticular Tumors

I. E. FORTUNY, M.D., A. THEOLOGIDES, M.D., Ph.D., and B. J. KENNEDY, M.D.

PREDNISONE OR URACIL MUSTARD used alone have been shown to be effective agents in the management of Hodgkin's disease, other lymphomas and chronic lympathtic leukemia.[1-13] During the early investigation of these agents, it was noted that certain patients with lymphoma, failing to respond to uracil mustard or prednisone alone, did demonstrate a response when these agents were administered concomitantly.[5,6,12] We, then undertook an investigation to compare the effectiveness of uracil mustard and prednisone, administered individually, sequentially, or in combination.

Patients and Methods

Sixty-three patients with the following disease were treated: Hodgkin's disease, 19; poorly differentiated histiocytic lymphoma (reticulum cell sarcoma), eight, other lymphomas (well differentiated and poorly differentiated lymphocytic lymphomas), 36. All the patients were in advanced, disseminated stages of their disease (Stages III and IV). Thirty-one of the patients had received radiation therapy previously, and upon reactivation of their disease, were included in the study (Group A); the remaining 32 patients had no treatment prior to entering the study (Group B).

Patients were randomly assigned (Table 1) to one of three drug schedules: uracil mustard alone, prednisone alone, or a combination of both. Uracil mustard was administered orally at a dose of 10 mg daily for three days. Prednisone was given in a daily oral dose of 40 mg for thirty days. The same drug doses and routes of administration were used for the combination schedule. Response to treatment was evaluated at four week intervals. When complete objective response was obtained, the drug cycle was repeated at six to eight week intervals for as long as the response could be maintained. Patients showing a partial response or failing to respond at the end of two or three evaluation periods after treatment with one of the drugs were placed on the other drug, and the response was evaluated at similar intervals.

Criteria for objective response were based on measurable changes of enlarged lymph nodes and tumor masses or healing of skin lesions. Disappearance of tumor masses or lymph nodes and healing of skin lesions constituted a complete response. Noticeable improvement of lesions, but without complete disappearance, was considered a partial response. Progression, or no measurable change in the observed lesions, was designated as a failure to respond.

Results

On the drug combination schedule 76.2% of the patients had an objective response, complete or partial, compared to 64.2% of patients responding to prednisone alone, and 60% to uracil mustard alone (Table 2). The differences are not

TABLE 1
Distribution of Patients with Lymphoreticular Tumors Treated by Chemotherapy

	Uracil Mustard	Prednisone	Both
Hodgkin's	8	6	5
Lymphoma	15	9	12
Reticulum cell sarcoma	2	2	4
Total	25	17	21

TABLE 2
Response of Lymphoreticular Tumors to Chemotherapy

	Uracil Mustard	Prednisone	Combination
Number of patients treated	25	17	21
Number of patients responding	15	11	16
Complete Regression	7	5	9
Partial regression	8	6	7
Percent	60.0	64.2	76.2

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statistically significant. The quality of tumor response was comparable in the three drug schedules (Table 2), although a more rapid response was observed in patients receiving the drug combination. There was no difference in the rate of response between the patients who had received irradiation previously (Group A) and the patients who had no treatment prior to entering the study (Group B).

The median duration of response for patients showing complete objective remission [and maintained subsequently by repeated courses every six to eight weeks] was 16 months for both the uracil mustard and the combination therapy group. In the prednisone only treated group the median remission was approximately of three months' duration. Once a remission was attained, maintenance was achieved by re-induction every six to eight weeks.

The breakdown in the response rate following the sequential drug regimen is shown in Table 3. Of the nonresponders and partial responders to the first drug, 50% responded partially or completely to the second drug. Of the patients who received uracil mustard as the second drug, two had complete remission of six and 10 months' duration respectively. Of those who received prednisone as the second drug, three had complete remission of two, three, and four months' duration. All these five patients were partial responders to the first drug; and none of the nonresponders to the first drug responded completely to the second drug.

TABLE 3
Response of Lymphoreticular Tumors to Sequential Drug Therapy

Initial Treatment			Response to the other drug (partial or complete)
Uracil Mustard	No response	10	3
	Partial response	8	6
Prednisone	No response	6	2
	Partial response	6	4

Discussion

The present study shows that in Hodgkin's disease, and lymphomas, uracil mustard and prednisone used alone can induce partial or complete remission in about 60% of the patients. In contrast to previous suggestions[5,6,12] the combination of these two drugs did not improve significantly the rate of response but probably induced a more rapid response than either of the two drugs used alone. This effect can be advantageous for a rapid regression of the tumor when the lymphomatous masses cause serious complications.

When a complete response was obtained by uracil mustard or the combination of the two drugs, the median duration of the control of the disease with repeated similar courses was by far greater than the median control with prednisone alone. A patient failing to respond to one of these two drugs has limited chances of responding subsequently to the other drug used alone.

Summary

In advanced Hodgkin's disease and lymphomas, prednisone and uracil mustard used alone produced similar rates of regression as their use in combination. With the combination, the induction of remission appeared to be more rapid. Patients who failed to respond to either drug alone had limited chances of responding to the other drug used subsequently.

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10-13. See page 728.

Concurrent Conditions and Diseases in Injured Persons

DONALD K. WHEELER, M.D. and EDWARD D. HENDERSON, M.D.

A SERIOUSLY INJURED person may have a concurrent disease that is undiagnosed or ignored because of the need for immediate treatment of the injury. Concurrent disease in an injured person frequently results in longer hospitalization and increased morbidity; it may even result in the death of the patient. Because this subject is frequently forgotten in practice and in the literature, this study was undertaken.

Method

In 1962 and 1963, there were 49,757 patient visits to the emergency room of St. Mary's Hospital in Rochester, Minnesota. Of these, 14,620 involved injured persons and 1,166 of them required hospitalization. Of these 1,166 admissions, 1,144 case records were reviewed; the remainder were incomplete or unavailable.

Injured patients were evaluated as to age, sex, residence, date and place of accident, cause of injury, nature of injury sustained, days of hospitalization, surgical procedures, known prior diseases, disease or condition contributing to the cause of the accident, concurrent disease that prevented surgical treatment of traumatic conditions, emergency surgical procedures performed for concurrent disease, deaths and causes of death.

Dr. Wheeler is a Resident in Orthopedic Surgery, Mayo Graduate School of Medicine (University of Minnesota), Rochester.
Dr. Henderson is from the Section of Orthopedic Surgery, Mayo Clinic and Mayo Foundation.

Analysis of Patients Hospitalized for Injury

Cause of Injury

In 1,144 patients there were 1,358 injuries, falls and car accidents being the most common causes of injury (Table 1). The relatively large number of farm accidents and injuries sustained while riding horses is related to the rural location of the hospital. Of the 470 patients who had falls, 51% were more than 50 years old; 28% of the patients injured by a fall were between the ages of zero and nine years. Fifty-one percent of the 302 patients injured in car accidents were between the ages of 10 and 29 years; 58% of burn victims and 78% of the persons struck by automobiles were between zero and 20 years old. Most athletic injuries, bicycle accidents, motorcycle accidents, and injuries sustained riding horses happened to persons less than 30 years old. The age distribution of farm accidents remained constant until 60 years of age.

Types of Injuries

The types of injuries at various ages are shown in Table 2.

Head injuries, comprising 27% of the total number of injuries, were subdivided into serious and minor injuries. If he had been admitted for observation for a few days but required no surgical or angiographic studies, the patient was classified as having sustained a minor head injury.

TABLE 1
Causes of Injuries According to Age Groups

Cause of injury	Age, year										
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
Total	235	263	138	71	85	91	97	93	58	13	1,144
Fall	127	56	12	15	19	56	62	65	48	13	470
Car accident	18	73	79	28	37	15	27	16	6	0	302
Hit by car	19	9	1	0	2	0	1	2	2	0	36
Horse accident	9	24	4	4	1	2	0	0	0	0	44
Farm accident	12	19	6	7	12	8	4	2	0	0	70
Sports accident	11	33	7	4	2	0	0	0	0	0	57
Bicycle accident	6	12	0	0	0	0	0	0	0	0	18
Hit by flying object	7	0	1	3	2	0	0	0	0	0	13
Machinery accident	1	2	5	2	0	3	1	1	0	0	15
Burn	13	8	2	2	4	2	0	5	0	0	36
Gunshot wound	0	6	3	0	2	1	1	0	0	0	13
Motorcycle accident	0	8	8	2	0	0	0	0	0	0	18
Miscellaneous	12	13	10	4	4	4	1	2	2	0	52

TABLE 2
Type of Injuries According to Age Groups

Type of injury	Age, year 0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
Total	257	305	188	81	114	110	104	123	62	14	1,358
Fractures	81	128	68	36	53	69	61	82	51	14	643
Head injury	119	90	44	21	24	21	21	15	5	0	360
Internal injury	3	13	8	2	5	2	4	3	0	0	40
Burn	15	7	2	2	4	2	0	5	0	0	37
Eye injury	1	4	1	0	1	1	0	0	0	0	8
Soft tissue injury	33	56	60	19	24	12	16	18	6	0	244
Miscellaneous	5	7	5	1	3	3	2	0	0	0	26

In this series, there were 135 serious injuries and 225 minor injuries; 31% of the serious head injuries required emergency surgical treatment. More than half of the head injuries occurred in patients less than 20 years old.

Most of the internal injuries were sustained in serious car accidents and farm accidents.

The majority of burns and injuries of the eye occurred in patients under 20 years old.

Fractures (excluding skull fractures) comprised 47% of the total number of injuries; the distribution according to body location is shown in Figure 1. The majority of fractures occurred in the extremities and were more common in the upper extremity than in the lower extremity, excluding hip fractures. The majority of upper extremity fractures were forearm fractures in young patients; the majority of the 106 hip fractures occurred in women over the age of 60 years. Emergency open reduction was required in 89 of the 643 fractures, and 155 nonemergency operative procedures were done. Some patients had several operations and several patients had multiple fractures; therefore the exact number of patients requiring open reduction of fractures was not determined.

Age and Sex Distributions of Injured Patients

In this series of 1,144 injured persons, 62% were males and 38% females (Table 3). There were more males than females among the patients 60 years old or younger; among those over 60, there were more females. Forty-three percent of the patients were between the ages of zero and 20 years.

Length of Hospitalization

The average duration of hospitalization was 11.6 days. It was least (average, five days) in the age group up to nine years and greatest (average, 23 days) among those over age 90. Among those more than 70 years old the average hospitalization was over 20 days.

Residency of the Patients

Of the 1,144 injured persons, 359 were from this city, and they came directly to the hospital. 597 were from surrounding areas in the State of Minnesota and, of these, 48% came directly to the hospital and 52% were referred by other physicians. The majority of those who came directly to the hospital were from nearby towns. 188 came from surrounding states (96% were referred patients and only 4% came directly to the hospital). The majority of patients who were referred by another physician were severely injured and needed extensive care.

TABLE 3
Distribution of Patients According to Age and Sex

Age (yr)	Males Number	Males Per cent	Females Number	Females Per cent	Total
0-9	154	66	81	34	23
10-19	185	70	78	30	26
20-29	112	81	26	19	13
30-39	52	73	19	27	7
40-49	58	68	27	32	8
50-59	53	58	38	42	9
60-69	42	43	55	57	9
70-79	34	37	59	63	9
80-89	17	29	41	71	5
90-99	3	23	10	77	1
Total	710	62	434	38	1,14

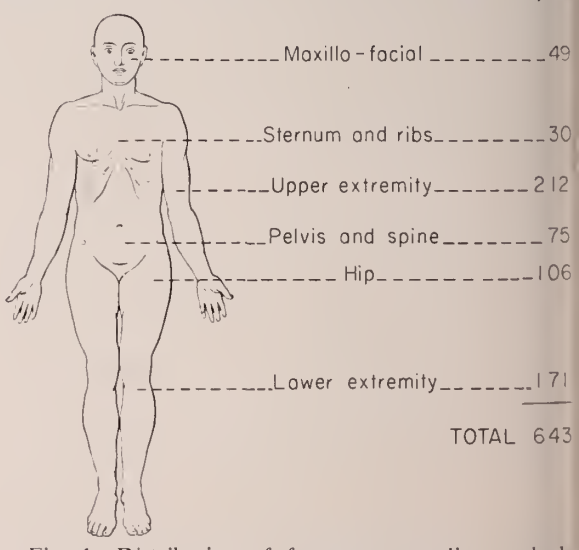


Fig. 1—Distribution of fractures according to body location.

Analysis of Concurrent Conditions and Diseases

Table 4 shows that in the 1,144 injured persons there was an overall incidence of concurrent conditions and diseases of 22%. The 10-to-19-year age group had the lowest incidence (4%) and the 90-to-99-year age group had the highest (85%). In general, the incidence of concurrent conditions or diseases increased with increasing age.

TABLE 4

Distribution of Concurrent Conditions and Diseases According to Age Groups

Age (yr)	Total number of patients	Concurrent condition or disease		Injury directly caused by concurrent condition or disease	
		Number	Per cent	Number	Per cent
0-9	235	12	5	0	0
10-19	263	11	4	4	2
20-29	138	19	14	14	10
30-39	71	18	25	9	13
40-49	85	11	13	3	4
50-59	91	26	29	8	9
60-69	97	47	49	8	8
70-79	93	57	61	10	11
80-89	58	40	69	3	5
90-99	13	11	85	1	8
Total	1,144	252	22.0	60	5.2

Distribution of Concurrent Conditions

Table 5 shows the distribution of the 349 concurrent conditions and diseases. The most common was the cardiovascular group (32%), most of whom were more than 60 years old. The most common metabolic disease was diabetes mellitus. The most common diseases among patients in the first decade of life were neurologic diseases and respiratory infections.

Acute alcoholism accounted for 75% of the concurrent conditions among those between the ages of 20 and 29 years.

Table 4 also shows that in 60 patients (5.2% of the total number injured) the concurrent disease or condition directly contributed to the cause of the trauma, and acute alcoholism was the most common of these (42 instances). Other concurrent conditions or diseases that contributed to the cause of the trauma were Parkinson's disease (four), vertigo (two), syncope (five), blindness (two), depression (two), grand mal seizure (one), and convulsion (one). These latter diseases and conditions were most commonly found in the older age groups.

Conditions Requiring Treatment

Of the 1,144 patients hospitalized for trauma, 107 had concurrent diseases or conditions that required further medical evaluation and treatment.* Emergency surgical procedures were delayed in 11 patients until the medical problem was attended to; the most common causes of delay were acute alcoholism, diabetes mellitus, and anemia.

Disease First Discovered

In 87 cases, the condition or disease was first discovered at the admission examination or during hospitalization for the accidental injury (Table 6). The two most common diseases found were cardiovascular disease and diabetes mellitus. The majority of these patients were elderly persons who had not visited a physician for several years prior to the accident.

Patients Requiring Concurrent Surgery

In two patients (66 and 88 years old), subtotal gastrectomy was done for perforated duodenal ulcers on the third and fourth days after surgical treatment for their injuries; both recovered and were dismissed after 18 and 39 days, respectively. A third patient had a perforated gastric ulcer on

*Acute alcoholism, 37; diabetes mellitus, 18; anemia, 14; convulsive disorders, 9; acute psychotic reactions, 5; heart failure and pulmonary edema, 4; parkinsonism, 3; tuberculosis of unknown activity, 3; delirium tremens, 2; hydrocephalus, 2; carcinoma with metastasis, 2; previous anticoagulation therapy, 2; infectious hepatitis, 1; gas gangrene, 1; Addison's disease, 1; bleeding duodenal ulcer, 1; severe rheumatic mitral stenosis with pulmonary edema, 1; and meningocele, 1.

TABLE 5

Distribution of Concurrent Conditions and Diseases According to Types and Age Groups

Condition or disease	Age, year										
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-99	Total
Total	12	11	20	20	14	34	67	88	64	19	349
Cardiovascular	0	1	0	1	4	9	23	36	29	8	111
Neurologic	5	2	3	3	2	2	5	14	7	1	44
Gastrointestinal	0	0	0	1	0	3	7	6	4	1	22
Malignancy	0	0	0	1	1	0	1	3	3	1	10
Genitourinary	0	0	0	0	0	0	3	0	0	0	3
Respiratory	4	0	0	1	2	2	5	7	4	2	27
Metabolic	0	1	0	3	1	6	11	12	7	1	42
Anemia	1	2	1	0	0	1	2	4	4	2	17
Alcoholism	0	2	15	9	3	6	7	5	0	0	47
Eye, ear, nose, throat	1	1	0	1	0	0	2	0	4	2	11
Psychiatric	0	1	1	0	1	4	1	1	1	0	10
Miscellaneous	1	1	0	0	0	1	0	0	1	1	5

the fourth day after admission and died in the hospital (day 26) from this complication.

TABLE 6
Conditions and Diseases First Discovered During Hospitalization for Trauma

Condition or disease	Number
Cardiovascular diseases	28
Diabetes melltius	12
Pulmonary diseases	10
Psychiatric conditions	6
Gastrointestinal diseases	5
Eye, ear, nose, or throat conditions	5
Anemia	9
Urinary infections	4
Thyroid diseases	3
Neurologic diseases	2
Malignancy	1
Gout	1
Liver disease	1
Total	87

Four patients had concurrent disease too severe to permit surgical treatment of their injuries (Table 7). All were elderly patients with fractured hips, and none lived more than six days after admission.

Deaths

There were 53 hospital deaths (36 among males and 17 among females), an overall mortality of 4.6%. Figure 2 shows that the age distribution of deaths closely paralleled that of injuries up to age 50 years, after which the death rate increased sharply.

Thirteen of the 53 deaths occurred within 24 hours after admission; the leading cause was severe head injury. Twenty-three patients died from their initial injury, most of them within 72 hours after admission. Thirty patients died from postoperative complications such as pulmonary embolus, bronchopneumonia, cerebrovascular accident, or concurrent diseases.

There were no deaths during surgical procedures, but three patients died during intubation for anesthesia prior to a surgical procedure; their average age was 74 years.

Discussion

The current philosophy of management c trauma is based mainly on military experienc acquired in two recent wars, but this experienc is limited in that, for the most part, it involve young men in good general health except for thei wounds. Such patients are the exception rathe than the rule in ordinary peacetime practic Life spans are longer, and hospital admissions c patients over 60 years are gradually increasin For example, between 1949 and 1959, admission for treatment of fractures in patients over 6 years increased from 39 to 54% at the Peter Ben Brigham Hospital.[1]

The yearly increase in the number of injurie and deaths in the home and on the highway i verified by the National Safety Council and simi lar organizations. Each year, over 40,000 death and 250,000 serious injuries occur on th highway.[1]

In a study of patients admitted to the Massa chusetts General Hospital for the treatment of a acute injury, Tannenbaum[2] found that more tha 25% had a concurrent disease of significant im

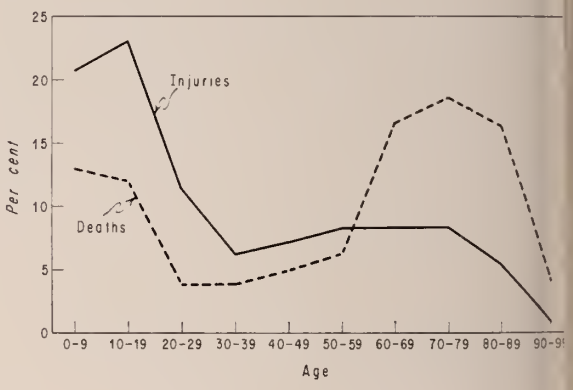


Fig. 2—Age distribution of deaths and injuries.

TABLE 7
Patients With Concurrent Disease Too Severe to Permit Surgical Treatment of Injury

Age (yr)	Injury	Disease	Treatment	Final outcome	Hospitalization (days)
95	Hip fracture	Cardiac; anemic	Blood transfusions; cardiac modification	Died with pulmonary edema	6
74	Hip fracture	Cardiac; chronic alcoholic	Cardiac medication	Died of esophageal abscess	4
93	Hip fracutre	Carcinoma of cecum	Supportive	Died of carcinoma	2
83	Hip fracture and head injury	Cardiac seizures	Supportive	Died with pulmonary edema	2

ortance, often previously unsuspected. He demnstrated that the association of concurrent disase with the production of accidental trauma can e quantitated. The incidences of concurrent disase in the patients we studied were almost idenal to those found by Tannenbaum, even though ur patients were private patients (his, ward paents) and our patients were from a fairly large rea (his, from a single metropolitan area).

Because of the high incidence of concurrent isease, when any injured person requires hospitalization a complete history should be taken and a complete physical examination, with adequate laboratory studies and roentgenograms, should be performed, all as rapidly as the emergency allows. There should be no exception to this practice if an anesthetic is to be given for a surgical procedure. Often the advice of an internist or pediatrician may be helpful for additional overall evaluation of a patient who is seriously injured.

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University of Minnesota

Course on Recent Advances In Infectious Diseases

The Department of Medicine and the Office of Postgraduate Medical Education of the University of Minnesota announce a course "Recent Advances in Infectious Diseases" to be held at the Mayo Memorial Auditorium on the Minneapolis Campus October 12 to 14, 1972 in honor of Wesley W. Spink, Regents' Professor of Medicine and Comparative Medicine.

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The Buckling Knee Syndrome

BROR S. TROEDSSON, M.D.

"Buckling Knee Syndrome" is a condition in which the patient complains of the knee giving way without any forwarning, and without the patient usually being able to give any definite cause. The case report may be cited as an example. The patient had had his left hip fused in 1954 and did well until June, 1970 when his left knee started to give way or buckle under him. All Xrays were negative except for the fusion of the hip. A neurological examination was negative. The patient was found to have tender and indurated areas in the left vastus lateralis, and rectus femoris (Figure 1). He had tried to strengthen his thigh muscles by exercises, but without any improvement.

To discover the changes in the muscles, which the patient as a rule is not aware of, it is helpful to grease the skin on both thighs with cold cream or cocoa butter. Both thighs are palpated simultaneously, and the tender, indurated areas in the muscles are then felt on the buckling side. Occasionally a patient may have buckling of both knees, and then the condition is felt in both thighs. It occurs in both men and women. The simplest case was that of a woman who was referred to us after a fall and who walked "stiff kneed" to prevent another one. In her case only the vastus lateralis area appeared involved, with the described induration and tenderness present. She was treated promptly with radiant heat and massage to the vastus lateralis area and recovered after five treatments. No other orthopedic diagnosis was entertained.

Since 1955 a total of 35 patients with a complaint of "knee buckling" or "giving way" have been seen. The ages were from 24 to 79. All but two were male veterans, the latter making up the bulk of the practice. Duration of complaint was from one week to fifteen years, average two years and ten months. Right side was involved in ten cases, left side in 21, and four were bilateral. The consistent finding in all of them was the tender hard oblong area in what appeared to be the midportion of the vastus lateralis.

Accompanying conditions or diagnoses were: Amputation of other leg (2), arthritis of knees (3), alcoholic neuritis (1), back and hip operation (2), bursitis of leg (1), chronic backache (1), diabetic neuropathy (1) had a fall (2), possible herniated disc (4), multiple sclerosis (3), muscular dystrophy (1), myotonia congenita (1), old disc operation (3), old postoperative subdural hematoma (1), old fracture of other leg (1), old cervical fractures (1), periarteritis nodosa (1), peripheral vascular disease (1), recovered old quadriplegia (1), Reiter's syndrome (2), residuals of fractured spine (1), and spondylolithesis (1).

All of the patients were referred to us either with one of the above diagnosis or with statements like these: "Has difficulty walking," "Weakness in leg," "Pain in lateral thigh," "Persistent leg pain," and "Status Post-L5-S1 hemilaminectomy." This shows the uncertainty about the diagnosis and the site of the trouble. The physiatrist has to take a detailed history and make a careful physical examination in order to find out the actual complaint and the location of the lesion.

The difficulties these patients have and the ease with which one can ascribe the symptoms to a concomitant condition is well illustrated by the oldest case.



Fig. 1—Area of tenderness and induration generally found in the lateral thigh in the Buckling Knee Syndrome.

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Presented at the Meeting of the Minnesota Physiatric Society on November 15, 1970 in Rochester, Minnesota.

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Case Report

A 79-year-old man, seen August 14, 1969, complained of his right knee buckling off and on for three ars. He had a brace on the right knee and used a rearm crutch to prevent falling (Figure 2). The history as long and involved, starting with a fall in 1941, llowed by backache and treatment of a "slipped" disc, ithout hospitalization. He was first seen at our hospital 1962, complaining of back pain and right leg pain d had 12 admissions from 1962 to 1969, inclusive. uring these admissions, the following diagnoses were ade: Chronic low back pain, possible herniated disc, to-scoliosis of lumbar spine, degenerative arthritis of ine and peripheral joints. In 1964, a myelogram was ne showing an extradural lesions at L3-L4 level. He as operated on for herniated disc, but none was und. Decompression was done. For a while his comaint disappeared, but then pain started on the side the right thigh and down to the knee. The knee was eak at this time, but did not buckle. It started to ckle in February, 1967. He had had many different rms of treatment without getting better. In June, 1968, had a McMurray osteotomy of the right hip with sertion of a Harris compression splint. This was moved in March, 1969. The knee still buckled under im in spite of the fact that he had had gait training nd strengthening exercises to his right hip muscles, ductors, flexors, and extensors. On examination, paent's knee was found to buckle at a flexion of 30-40°. oth quadriceps muscles were found strong, the left ightly stronger than the right, but with adequate rength. Slight but equal crepitation was present in oth knees, but there was no swelling or tenderness round either. Careful palpation of the right thigh uscles disclosed (with the skin oiled,) a four-inch long nd half inch wide, tender, thickened area in the midortion of the lateral thigh. This appeared to be in e vastus lateralis portion of the quadriceps femoris uscle. There was not any such area on the left side. here was an operative scar over the right hip and ver the lumbar spine. Muscle strength test showed a trength of 31½ pounds in the right quadriceps and 37 ounds in the left. A diagnosis of fibrositis of the right astus lateralis was made. The patient was started on adiant heat and massage to the right vastus lateralis nd isometric progressive resistance exercises to the uadriceps femoris muscle complex. After five treatnents, the patient could walk around without his knee race and with only very little support from his Canaian crutch. The quad strength measured 41½ pounds ilaterally at this time. Treatment was continued with icycle exercises added, until he had a total of 18 reatments. He could then walk around on flat ground, p and down ramps, up and down stairs without the nee buckling. He still felt a little unsure of himself ecause his balance was poor and he liked to carry a ane around as a safeguard. The quadriceps strength t this time was 46½ pounds. The patient was disharged one month after admission. He was seen again ix weeks later and had had no recurrences of his knee uckling.

The buckling or giving way of the knee has been described as occurring in many conditions. Thus, Rosenblum, et al,[1] described a number of cases, cited other authors, in which the condition had followed hysterectomy. They ascribed the condition to pressure of the retractor blades on the greater psoas muscle with production of ischemia of the femoral nerve supplying the quadriceps femoris. They stated that the neural condition needed to create little concern, for it was almost always reversible. Our cases, of course, were not of this nature and presented no evidence of detectable femoral nerve pathology. Other conditions in which buckling of the knee has been present are cited by many authors. Thus O'Donoghue[2] and Cane[3] point out its possible presence in injuries to the menisci, but with it there is also a history of injury, local tenderness, pain and swelling of the knee. Our cases did not fall in this group either, but showed only one uniform finding of tenderness and induration in the vastus lateralis area. In spite of diligent search of the literature, we have been unable to find any reference to this condition. It is not mentioned by Steindler,[4] Mercer,[5] or Reno[6] under our sympto-



Fig. 2—A 79-year-old man with a buckling knee for two and a half years used a knee support and a crutch to prevent falling.

matic diagnosis of "Buckling Knee." We have not been able to find any reference to this condition under our pathological diagnosis of "Fibrositis." It is not mentioned by Adams,[7] Buckley,[8] Collins,[9] or Slocum.[10]

In investigating this distinct condition we had electromyograms done on two patients. There were no abnormal findings. A biopsy of the vastus lateralis on one case showed no abnormal findings.

Our observations lead us to believe that some loss of strength in the affected thigh may be due to disuse. Buckling of the knee occurred in those cases where we measured it at a knee flexion of 25° to 40°. We have under observation one patient who has had a buckling knee since 1962. He has been seen frequently, has not had any treatment and still has his buckling knee with the typical tenderness and hardness on the lateral side of the thigh.

It is our opinion that skillful massage is most important. One patient had had many kinds of previous treatments, whirlpools, diathermy, strengthening exercises, walking, medications, injections, and an operation, without any essential improvement. With heat and massage, the hardened area could be felt to decrease in tenderness and size until it was practically gone. We used strengthening exercises also. In regard to the location and the nature of the lesion that we are dealing with, we consider it to be a so-called *fibrositis* of the vastus lateralis of undetermined etiology. It feels like other fibrositic areas occurring in neck, back and leg muscles. It responds to heat and massage as other fibrositic muscles do. The process may involve the intermuscular septum and the muscle origin on the femur and may also involve the vastus intermedius and the iliotibial band. To us it seems that the primary lesion is in the vastus lateralis. As to the causative factor we can only speculate. The process does not seem related to any neurological condition or we would find it consistently associated with neurological findings. We have always thought it to be in the nature of an inflammation, but our one biopsy failed to show this condition, though that does not rule it out. The possibility of a virus, a local allergy, an enzymatic or some local metabolic disturbance is a possibility. In a way, the condition acts very much like an epicondylitis in the elbow. In this condition the patients suddenly drops something that he is holding, such as a glass of water. There is no pain, no premonitory sign. When examined, these patients have a hard tender area in the wrist extensors and tenderness over the lateral epicondyle of the elbow. Individual muscles in the forearm are found amply strong to hold a glass of water. However, in some way at a certain point there is an interruption in the neurological co-ordinating mechanism, the muscles lose their power momentarily, and the glass drops out of the hand. The same mechanism seems to be present in the Buckling Knee. There is a controversy as to the nature of these lesions. They are called fibrositis, myositis or muscle spasm, and their existence is denied by some. However, they do exist and are capable of causing great disability as demonstrated by many of our patients. Of the 35 cases seen, we had the opportunity of treating 25. Only one did not get much better. He was a post-hemilaminectomy case with bladder and bowel difficulties and tenderness over the sacro-iliac joints, in addtion to his vastus lateralis tenderness. After four and a half weeks of treatment he estimated he was 25% better. The other 24 patients improved to the point where they could discard wheelchairs, crutches, walkers, canes and the knee did not buckle any more.

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Each generation has to find out for itself that the stove is hot.

Obstructive Airway Disease

Resting and Post-Exercise Spirometry

NELSON A. PAGUYO, M.D., SUMNER S. COHEN, M.D. and
JEROME T. GRISMER, M.D.

THE PHYSIOLOGICAL BASIS of exercise has been studied by numerous investigators since the recognition of it's beneficial effects in normal subjects.[8,19] The rationale of its use as an adjunct in total management of patients with cardiac, vascular, respiratory, musculo-skeletal and cerebral abnormalities has been extensively discussed in the literature. Barach,[2] Itkin,[9,10] Miller,[11] Naughton,[12] Paez[13] and Pierce[16] have shown the advantageous effects of exercise in the treatment and rehabilitation of patients with various pulmonary diseases.

Although the precise mechanism of improvement following exercise is not known, certain explanations have been advanced. These are:[13,16] (1) increase in muscular efficiency, (2) increase in neuromuscular co-ordination, (3) improvement in cardiac, pulmonary, and vascular functions, (4) increase in efficiency of the neuropituitary-adrenal axis, and (5) possible changes in the balance between aerobic and anearobic metabolism due to a more active oxidative process during exercise.

Materials and Methods

All patients in the Emphysema-Chronic Bronchitis Clinic having their routine trimonthly followup examinations from June 11, 1969 to November 11, 1969 were included. A total of 96 cases were analyzed. These patients had been followed from nine to 30 months and were considered proficient in the use of the treadmill and the Stead-Wells Spirometer.

A trimonthly followup consisted of a brief review of the patient's history, complaints, clinical progress, medications, physical examination, resting spirometry and treadmill exercise. The study included essentially the same procedures except with the addition of an immediate post-exercise spirometry performed within five minutes after completion of the treadmill exercise.

The ability to perform treadmill exercise varied widely from patient to patient. However, each patient was encouraged to accomplish to their maximum exercise tolerance.

Resting and post-exercise spirometry were then compared. Indirect maximum voluntary ventilation (MVV) was calculated with the formula introduced by Kennedy[6] $MVV = FEV_{0.75} \times BTPS \times 40$. (FEV is forced expiratory volume and BTPS means body temperature, pressure, saturation.)

A 10 percent or greater change between the resting (control) and post-exercise values was arbitrarily considered significant. The patients

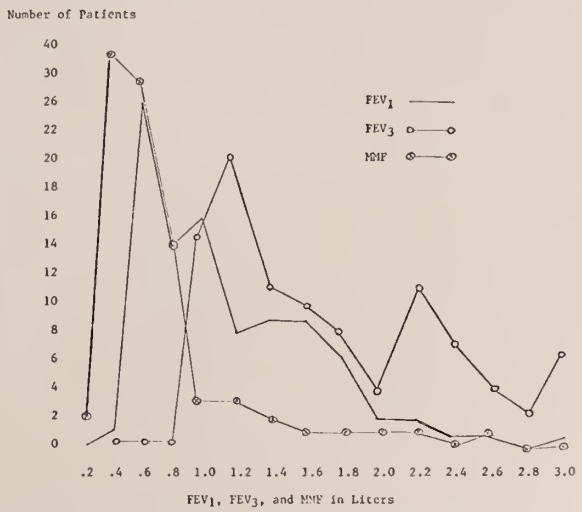


Figure 1—Patient distribution in the resting stage, One-Second Forced Expiratory Volume (FEV_1), Three-Second Forced Expiratory Volume (FEV_3), and Mid-Maximum Flow Rate Plotted Against the Number of Patients. Fifty-six patients are in the range between 0.6 to 1.0 Liter FEV_1, 55 between 1.0 to 1.6 Liter FEV_3 and 67 between 0.4 to 0.6 Liters MMF.

Mount Sinai Hospital Emphysema-Chronic Bronchitis Clinic.
Dr. Paguyo was Project Physician.
Dr. Cohen was Project Consultant.
Dr. Grismer was Project Director.
Supported by the Department of Health, Education, and Welfare, Chronic Disease Section, Contract Number P.H. 108-16-146.

were then classified as: (1) Group A. those who demonstrated 10 percent or greater improvement, (2) Group B: those who remained relatively unchanged, and (3) Group C: those who became worse by 10 percent or more.

Results

The data are summarized and illustrated as follows.

Figures 1 and 2 describe the severity of the obstructive disease in the group studied. More than 55 percent of the cases fell within the following ranges; (1) One-second forced expiratory volume (FEV_1) 0.6 to 1.0 liter; (2) Three-second forced expiratory volume (FEV_3) 1.0 to 1.6 liter; (3) Maximal mid-expiratory flow rate (MMFR) 0.4 to 0.6 liter; (4) Maximum voluntary ventilation (MVV) 15 to 30 liters per minute.



Figure 2—Patient Distribution in the Resting Stage—Maximum Voluntary Ventilation. Fifty-four patients are between the ranges of 15 to 30 liters per minute.

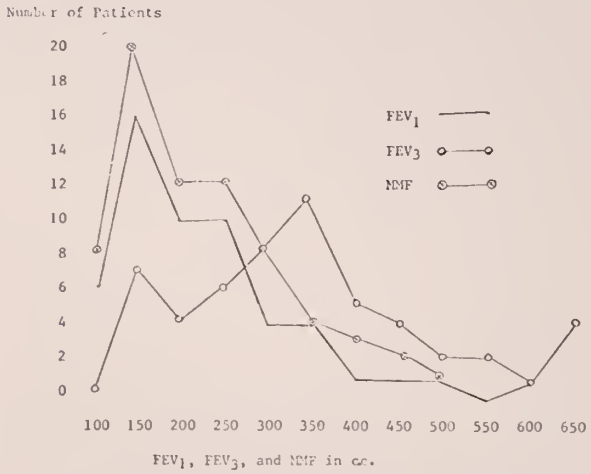


Figure 3—The Range of Improvement of Patients in Group A. The difference between the resting and post-exercise spirometry of Group A is plotted against the number of patients.

Table 1 summarizes the distribution of the patients into the three groups after exercise. 67 percent, 56 percent, 70 percent, and 60 percent of patients studied improved in FEV_1, FEV_3, MMFR, and MVV respectively.

Table 2 shows the average changes of the three groups after comparing the resting and post-treadmill spirometry.

Table 3 is a comparative study of the mean values of the 96 resting spirometry (control), the resting spirometry of the improved group (Group A) and the actual improvement of Group A following exercise.

Figures 3 and 4 illustrate the ranges of the difference between resting and post-exercise values of Group A patients along the ventilation parameters analyzed.

Discussion

The patients included were all diagnosed emphysema and/or chronic bronchitis. The majority represented advanced chronic obstructive airways disease with functional classification of III to V. Prior to this study, these patients had intensive treatment consisting of oral drugs, inhalation and physiotherapy. Regular physical exercises were stressed to the patients as an important factor in rehabilitation from the time they were started on the treatment program. After nine to 30 months of therapy, a significant segment of our patients were still unimpressed with the beneficial effects of regular physical exercise.

The effect of exercise was studied by a comparison of resting and immediate post-treadmill spirometry. The initial findings in a few patients were considered significant so that the study was extended.

The data (Table 3) indicate that the resting spirometry values of the patients in Group A are lower than those of the control. This implies that the patients who actually improved with exercise are the most advanced cases in our study group. The mechanism of this improvement is not known. Based on previous findings, however, one can only present theories possibly explaining the above observations.

Refsum[17] studied the respiratory response to

acute exercise and found that there is a remarkable increase in ventilation, which is due primarily to an increase in tidal volume. Briscoe,[3,4] Cohn,[5] Penman[15] and many others have documented the existence of a spectrum of regional ventilation-perfusion imbalance in patients with chronic obstructive airways disease (C.O.A.D.). This inequality between the alveolar ventilation and pulmonary capillary perfusion apparently is most pronounced at rest and improves with exercise.[5] This uneven ventilation-perfusion ratio may be sufficient to produce hypoxemia which in turn causes increased airways resistance in patients with C.O.A.D.[14] In view of these observations, one can presume that the increase in the post-treadmill exercise spirometry of patients in Group A can be explained satisfactorily on the basis of increased ventilation, improvement in ventilation-perfusion ratio and relief of hypoxemia to near normal or normal levels resulting in decreased airways resistance and possibly relaxation of bronchospasm.

Another explanation that can be advanced involves the concept of alpha and beta adrenergic receptors, first proposed by Ahlquist.[1] According to this concept, stimulation of the alpha receptors leads to a variety of reactions including constriction of vascular smooth muscle and increased automaticity of the heart. Stimulation of the beta receptors, on the other hand, results in an increased chronotrophic and ionotrophic action of the heart, bronchodilation and relaxation of

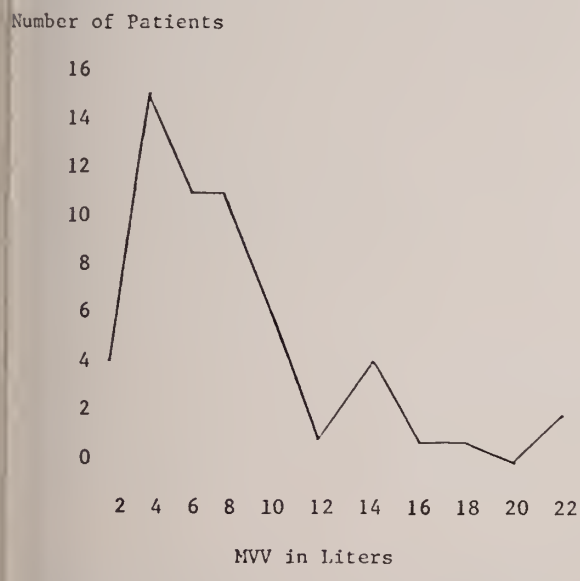


Figure 4—Distribution of Group A patients with their improvement in liters per minute after exercise.

TABLE 1

Classification of Patients After Exercise. Comparing the resting and post-treadmill exercise spirometry, patients were categorized into Group A (10% or more improvement), Group B (unchanged), and Group C (10% or more worse). The Table shows that the majority improved and a very few became worse.

Classification	FEV_1	FEV_3	MMF	MVV
Group A	55 (57%)	54 (56%)	70 (73%)	58 (60%)
Group B	37 (39%)	39 (41%)	20 (21%)	37 (39%)
Group C	4 (4%)	3 (3%)	6 (6%)	1 (1%)

TABLE 2

The Averages of the Changes in Spirometry Tests of the Three Groups after Exercise. The differences between the resting and post-exercise spirometry were obtained and averages determined. The plus (+) and minus (−) signs before the numbers designate the average improvement or deterioration of each group.

Classification	FEV_1/cc	FEV_3/cc	MMF/cc	MVV/L
Group A	+204	+319	+201	+8.0
Group B	+ 46	+ 51	+ 6	+1.4
Group C	−152	−213	−270	−8.6

TABLE 3

Comparison of the Average Values of the Control, Group A, and Actual Improvement in Group A.

	FEV_1/cc	FEV_3/cc	MMF/cc	MVV/L
Control	1022	1650	560	34
Group A	845	1472	485	30
Average Improvement	204	319	201	8.0

the vascular smooth muscles. The catecholamines (norepinephrine, epinephrine and isoproterenol) may be divided as an alpha or a beta stimulating agent. Norepinephrine is mainly an alpha receptor stimulator and isoproterenol, a potent beta receptor agent. Epinephrine acts on both alpha and beta receptors.

With the advent of a histochemical fluorescence technique for the localization of monoamines,[7] Weiner[18] recently reported that the bronchial smooth muscles are sparsely innervated by adrenergic neurons. Adrenergic neuron apparently stores norepinephrine which is released by stimulation of the nerve. Weiner postulated that under stress situations, cathecholamines, notably epinephrine, are discharged from the adrenal medulla. Because of the rich vascular supply of the bronchial tree, epinephrine is more likely to reach the bronchial muscles in higher concentration than the norepinephrine released from the scantily distributed adrenergic neurons. The result is more of bronchodilation than bronchoconstriction.

The exercise imposed on our patients constitutes a form of stress situation. This may explain why the most advanced cases in our study showed significant improvement following treadmill

exercise.

Summary

Ninety-six patients with proven chronic obstructive airways disease were studied. Resting and immediate post-treadmill exercise spirometry were compared. More than 55 percent of the subjects improved. Those who improved constitute the more severe cases. An explanation of this phenomenon is discussed.

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'Tis a small matter in your neighbor's case,
To charge a fee for showing him your face;
You skip up-stairs, inquire, inspect, and touch,
Prescribe, take leave, and off to twenty such.
But when at length, by fate's transferred decree,
The visitor becomes the visitee,
Oh, then, indeed, it pulls another string,
Your ox is gored, and that's a different thing!*

*Oliver Wendell Holmes, Sr., "The Morning Visit," 1849.

Psychiatry

The Suicidal Physician

WERNER SIMON, M.D.

WHY DO PERSONS in a profession in which the goal is preservation of life kill themselves? Blachly et al.,[1] who have done a great deal of work on this subject, present some factual data. In a study published in the Bulletin of Suicidology, from May 1965 to June 1967, they reported that suicide was the cause of death of 200 of the more than 7,500 physicians who died. The average age of the suiciding physician was 49; the preferred method was the use of drugs; the average incidence was 36 per 100,000 among physicians compared with an average incidence among the average population of 11 per 100,000. The lowest incidence among the specialities was among pediatricians—10 per 100,000; the highest incidence was among psychiatrists with 61 per 100,000. In breaking down some of Blachly's figures, one finds the distribution among various medical schools of great interest. It so happens that the University of Minnesota provided the highest figure with 10; next to this Colorado with 8; and then Illinois, Harvard, and Pennsylvania with seven each. When one examines these figures more closely, one finds that certain graduating classes from particular years form definite clusters. For instance, in Minnesota the years 1934 to 1936 provided most of the completed suicides.

Physician Suicide at Veterans Hospital

Several years ago we studied at our hospital suicide among physician-patients.[2] We had 36 physicians as psychiatric patients and were very much interested in the outcome of our treatment for our follow-up information. We were aware of the increasing incidence of suicide among physicians and noted the trend with mounting concern. A survey of patients treated on the In-Patient Service at our hospital, covering a span of 20 years, revealed that 36 physicians had been patients and follow-up inquiries yielded the information that five of them, or 13.8%, subsequently committed suicide. We made a special study of these five patients to elucidate any factors which might have been useful in predicting the high suicide risks among them in contrast to others who revealed suicidal preoccupation during their hospitalization but did not commit suicide. In other words, we did what is currently known as a "pychological autopsy." We studied them with Minnesota Multiphasic Personality Inventory (MMPI) profiles and found the group profile for the physician-patients who had suicidal preoccupation to be in marked contrast to that found in other studies of suicidal preoccupation. The physician-patients differed from other psychiatric patients with suicidal preoccupation in that the physician-patient tended to deny personal distress or psychological discomfort. The propensity toward suicide in the physician-patients seemed to be well covered and in this sense made them much more difficult treatment prospects. Three of our five patients who committed suicide had a diagnosis of manic-depressive illness; they had many recurrent episodes, had had much intensive therapy, and suicide for them could have been interpreted as one possible response to insoluble emotional problems. This was before lithium therapy had been introduced. Nowadays with lithium the outcome might have been different, as newer studies[3] indicate that lithium is capable of preventing recurrent episodes of manic-depressive disorder. The other two suicides carried the diagnosis of personality disorder and were characterized by episodes of acting-out behavior. These patients showed marked defensiveness in admitting their psychological problems and because of their elaborate denial system closed themselves off to any therapeutic intervention. These two diagnostic catagories, according to our study of physician-patients, constitute a high suicidal risk. None of our neurotic patients committed or even attempted suicide. Also, and this was somewhat surprising to us, no schizophrenic patient in

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our study ended his life by self-destruction.

In another investigation[4] we studied these same patients from the standpoint of alcoholism and drug addiction, which we considered a possible attempt at chronic self-destruction. Since the rate of suicide was 13.8% among our physician-patients and this figure is higher than the 8-9% suicide rate cited in earlier reports for physicians who were drug addicts, it seemed that drug addicts do not commit suicide as frequently. It is well known that the incidence of drug addiction among physicians is much higher than in the general population, both in the United States as well as in Europe, and it has been called an occupational hazard. In our investigation, we found the incidence of alcoholism and drug addiction among our hospitalized physician-patients to be very high. The figure for alcoholism was 69% and for drug addiction 58%, much higher than in any other reported studies. Thus it appeared that alcoholism and drug dependence were much more frequent among physicians who are veterans. One might well speculate that the rate is most likely to be much higher for veterans returning from Vietnam. Alcoholism and drug addiction occurred in the following diagnostic groups in order of frequency: (1) neurotics, (2) personality disorders and (3) psychotics. Again, we found that addicted physician-patients generally were markedly defensive and had a very elaborate denial system closing themselves off to any effective therapeutic intervention. An assessment of this defensiveness was attempted with a special research scale in the MMPI. This proved to be the highest for those patients with histories of addiction and lowest with no such history. This could be explained on the basis of omnipotence, through feelings of being immune to death or suicide. Cantor[5] has pointed out that certain forms of death-play are not recognized by society as suicide but are permitted as normal behavior to overcome the fear of death. Such play, for instance sustained alcoholic intoxication, can become a suicidal equivalent. However, if one can break through this defensiveness and get physician-patients to admit their psychopathology, the outcome appears to be more favorable. This is fortunate, as suicide is irreversible, whereas drug addiction can be reversible. Initially patients will deny that their addiction is a suicide substitute or that they have any psychological problems, but later in retrospect they will often acknowledge and recognize their death wishes. At times, addiction may appear to have a hopeless prognosis to patients and their families. However, our study shows that as many patients with good outcome on follow-up had histories of chronic alcoholism and/or drug addiction as did poor outcome patients. Our findings support the results of Small et al.[6] who report that almost half of the alcoholic and drug-dependent physicians return to regular full-time medical practice.

The Suicide-Prone Physician

When one asks the question how does one recognize a physician who is in danger of suicide or who is contemplating suicide in order to take steps to intervene or to prevent this tragedy, various authors give us different clues as to how to recognize such symptomatology.[7,8] For instance, suicide-prone physicians often seem more interested in their work than in their home lives and they frequently neglect their wives and children. They very commonly have marital problems. It is true that long hours of practicing can cause in some people considerable exhaustion so that they are unable to share the daily concerns of wife and children. When the physican's wife pleads with him to take more time away from work, this can lead to further problems and conflicts. Being married to a practice becomes particularly risky for physicians with a tendency toward self-destruction.[9] When one considers that physicians are on-call 24 hours a day and are expected to perform at maximum efficiency at all times—this puts the physician under great physical and psychological stress—more so than members in other professions. Many physicians turn to drugs because of overwork and pressure. The progression from severe practice demands to stimulants and to eventual self-destruction has also been outlined by Blachly[1] as beginning with annoying physical symptoms and leading to severe mood swings, reluctance to accept society's restraints, and finally dependence on drugs or alcohol. Not all drug or alcohol abusers end in suicide, nor do all suicides have a history of such dependence, but the correlation is quite common. Litman[10] of the Los Angeles Suicide Prevention Center, estimates that about half of all physician suicides are preceded by misuse of alcohol or drugs or both.

How does one recognize the suicidal physician if he uses drugs? It is difficult unless he is caught red-handed. He finds it hard to ask for help

because he might consider it weakness. If he decides that he must take action, he usually will not go to another doctor but rather treat himself. He will not admit to his wife that he is dependent on drugs. He will absolutely refuse to see a psychiatrist. Neither will he confide in a family physician or colleague friend for fear that word might get around and his license might be suspended. When he tries to interrupt his habit, the result is usually withdrawal symptoms, severe depression and guilt, and soon he goes back on drugs as an emotional crutch to combat these symptoms and often then is forced to increase his former dosage.

There is an important age factor. A high risk period, for instance, occurs when a young physician leaves the protected environment of residency to face the responsibility of establishing himself in practice. Another high risk period exists when the physician nears retirement and he may view life as not worth living without the gratification he has had from his medical career. The average age of maximum stress and anxiety for many physicians is 49, according to Blachly.[1] It is the time when parents are dying, when children are leaving the home, when chronic marital difficulties become more intense, and competition of younger colleagues is becoming apparent.

The Danger Signs of Suicide

What are the warning signs which can be detected? If a physician has a close relationship with a colleague, an associate, or a personal friend, then it might be easier to communicate his feelings and possibly his preoccupation and intent. The physician who is a particularly high risk for potential suicide is one who has suffered severe personal loss, such as a death in the family, divorce, loss of health, professional reversals, and diminished prestige. The outward manifestation and symptomatology may be apathy, loss of appetite, depression, loss of weight, insomnia, agitation, sometimes outwardly noticeable changes. Giving away possessions which have meant a great deal, or making statements such as the family might be better off without him, can be revealing. Personality changes can be apparent,[11] even to other colleagues, but what is usually quite obvious is the over-use of alcohol and drugs. Signs in appearance and behavior occur which make the knowledgeable person suspicious: inability to remember clearly, tremors, extreme signs of fatigue, carelessness about dress, slurred speech, difficulty in talking, overuse of amphetamines, refusing to rest or relax. He becomes forgetful, uses unusual therapeutic procedures which do not seem to be indicated, and his attention wanders when a discussion is attempted.

Physicians deny any sign of their own illness and colleagues hesitate to intervene. If one can break through the defensiveness and encourage physician-patients to admit their psychopathology, the outcome is more favorable. How can this be accomplished? Most drug-dependent patients use the technique of a pattern of self-defense called procrastination supported by a system of rationalization. Since this is largely a conscious type of defense mechanism, it should be attacked directly by confrontation before psychotherapy is begun. The success of doctors' groups with Alcoholic Anonymous begins with the liquidation of the "alibi system." Inasmuch as physicians are familiar with all the physical, neurological and cerebral complications of alcoholism and drug addiction, it would appear that addiction is deliberate self-destruction for them. However, many therapists treating physicians assume that "the doctor ought to know" and do not prescribe definite treatment as if expecting self treatment. It is essential that a trust relationship be established in which it is safe for the physician-patient to surrender himself into the care of his therapist, overcoming denial, and giving up any omnipotent traits. Sometimes a successfully treated physician "who has been through it" becomes a most effective therapist. It may be helpful to bridge the gap by allowing the physician-patient to be a cotherapist in his own treatment by individualizing his own medication in the face of anticipated stress situations, as Small and others[6] have suggested. But this can also be a risky procedure. It must be remembered that practically all of the alcoholic and drug-dependent physician-patients are depressed and should be treated for depression, once a break-through of the defensiveness is accomplished. Initially the patients will often deny that their addiction is a suicide substitute or that they have any psychological problems. Later on, in retrospect, they will often acknowledge and recognize their death wishes.

Treatment

Getting a troubled physician to admit that he needs professional help, and then to seek it, is a hard step to take. If he finds someone he can

trust, with whom he can ventilate his feelings and disclose his moods and disappointments, it becomes much easier. Blachly[12] is in favor of confrontation and believes it can be effective. He proceeds subtly by indicating that he knows something is wrong and asking if he wants to talk about it. He states that a surprising number of physicians have been talked out of suicide by being made aware of the economic and realistic consequences of such an act. Many lives could be saved if we were not prone to stop short of such difficult but often necessary extremes as hospitalization, shock treatment, or even arranging for possible legal action such as commitment.

The emotional screening, education and self-awareness should begin, not at age 49, but in medical school. Schofield[13] has studied medical students at the University of Minnesota and describes the future physician who is in danger when looked at as a freshman or junior medical student. Their MMPI profiles might be predictive of future maladjustments. He found that with aptitude variance controlled, the underachievers were characterized by "a tendency toward unrealistic appraisal of their environment, unhappy social relationships, and autistic ruminations." These same underachievers also showed general tendencies toward relatively unsophisticated denial of personal weakness and the expression of idealized self-concept. Such persons may be expected to respond to intense role strain with increased vulnerability, and if the paranoid defensiveness scale is found to be elevated, one might hypothesize an increased liability toward suicidal preoccupational behavior.

What psychopathology do physicians who later on commit suicide show? Modlin and Montes[14] studied their physician-patients at the Menninger Clinic and found that as children they had been sickly; that in adolescence they were very studious, ambitious, and did well scholastically; but their married lives were depicted as ambivalent an dependently attached with much marital an sexual conflict. Their personalities were describe as basically insecure with unrealistic aspiration and vulnerable self-esteem. They denied any lim itations, although showing many signs of fatig ability and energy-draining neurotic struggles, re sulting in becoming tired of giving and ambivalen toward medical practice. Duffy,[15,16] who studie physicians admitted to the Mayo Clinic as psychi atric patients, reported that denial was a commo mechanism in therapy, with overt hostility towar the therapist quite frequent, manipulation of th environment with many demands, and the use o alcohol and drugs as a defense against overwhelm ing anxiety were common. The extreme resistanc to admitting his psychopathology and acceptin psychiatric treatment seemed most characteristi of these physician-patients.

The problem of the emotional health of physi cians has become so much of a concern that special panel of psychiatrists considered this topi at the 1967 American Psychiatric Associatio meeting. Medical societies in their regular meet ings should have special symposia where thi occupational hazard, suicide among our col leagues, should be considered and discussed Physicians are no more immune from emotiona problems then they are from physical illnesses Many professional "suicidologists" recommen an annual emotional check-up. Many medical so cieties send out annual reminders for regula physical examinations to their members and i would be a good idea to include an emotiona inventory at the same time. Industry has begu to think in terms of psychological examinations a regular intervals for their executives, and th Menninger Clinic, for instance, has many indus trial executives going there each year for an emo tional check-up. The same thing can be don for physicians.

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The following patient profiles represent typical clinical situations, but do not necessarily represent actual cases.

Age 22, previously normal me
with occasional menorrhagia
on a sequential O.C. for four r
Complains of heavy flow,
occasional intracyclic bleedin
edema, tender swollen breast
Indicates estrogen excess
1st choice: Switch to a com
bination 50-mcg.-estrogen O
(such as **Demulen***).

Age 19, small breasts, minor hirsutism, oily hair and skin. History of metrorrhagia, skipped or scanty menses. New user.
Indicates androgenic excess or estrogen deficiency (fertility is suspect).
1st choice: An estrogen-dominant O.C. (such as **Enovid-E***).

Age 25, average frame, poor complexion. No problem with menses, normal para 1. On a low-estrogen/high-progestogen O.C. for two years. Now complains of scanty flow, decreased libido, depression.
Indicates probable buildup of progestogen-related side effects.
1st choice: Switch to a center-spectrum O.C. with more estrogen, less progestational activity (such as **Ovulen***).

Age 21, short, mammose, with normal menses, some acne. Was put on prenuptial regimen of 50-mcg.-estrogen/moderate-progestogen O.C. for two months. Now has increased acne.
Indicates metabolic production of androgen or relative estrogen deficiency.
1st choice: Switch to a 100-mcg.-estrogen combination (such as **Enovid-E*** or a sequential).



Unmasked, physiologically and anatomically, they're not all the same. A basic difference lies in their hormone profiles. One may secrete too much estrogen, another not enough...or perhaps too much androgen; the vast majority would fit somewhere into the broad center spectrum.

Although the profiles described below may not be completely predictive, in optimal O.C. selection, the estrogen-progestogen activity ratio should be carefully matched to the patient profile. Searle offers you O.C.s in a range not only suitable for your patients in the balanced center spectrum, but also adaptable to the patient with another type of hormone profile.

Oral contraceptives are complex medications. Among the commonly reported adverse reactions are: intracycle bleeding, fluid retention, tender or swollen breasts, exacerbation of acne condition, changes in libido, amenorrhea while on medication and upon discontinuance, nausea, leg cramps, headaches, weight gain. Therefore, after reference to the prescribing information, oral contraceptives should be prescribed with care.

*Note: In some patients any level of exogenous estrogen or progestogen may produce symptoms of excess hormone activity.

'5, tall, slender, athletic,
flat chest. On a progestogen-
nant 50-mcg.-estrogen O.C.
ecurrent trichomoniasis
Monilia.
dicates estrogen deficiency and
ss of progestogen in current O.C.
t choice: Switch to a com-
ion pill with 100 mcg.
s gen and less progestational
ity (such as **Enovid-E*** or
Ov en* or a sequential).

Age 23, "Miss America" figure, previously normal menses, healthy skin and hair. On a 50-mcg.-estrogen pill for four months. Complains of intracyclic bleeding.
Indicates probable need for more estrogen.
1st choice: Switch to a center-spectrum O.C. with more estrogen and moderate progestogen dominance (such as **Ovulen***).

Age 21, college senior, average build. On highly progestogen-dominant/low-dose-estrogen O.C. for six months. Now complains of amenorrhea, between-cycle headaches, weight gain.
Indicates probable progestogen excess.
1st choice: Switch to a center-spectrum pill (such as **Ovulen***).

Age 27, slightly overweight, multiparous. Nausea with all three pregnancies and with a sequential O.C. three years ago. Has pre-menstrual fluid retention and leg cramps.
Indicates probable excess of estrogen.
1st choice: A 50-mcg.-estrogen/progestogen-dominant pill (such as **Demulen***).



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Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

Actions – Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note – Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication – Ovulen and Demulen are indicated for oral contraception.

Contraindications – Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings – The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[1] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions – The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives – A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

References: 1. Royal College of General Practitioners: Oral Contraception and Thrombo-Embolic Disease, J. Coll. Gen. Pract. *13*:267-279 (May) 1967. **2.** Inman, W. H. W., and Vessey, M. P.: Investigation of Deaths from Pulmonary, Coronary, and Cerebral Thrombosis and Embolism in Women of Child-Bearing Age, Brit. Med. J. *2*:193-199 (April 27) 1968. **3.** Vessey, M. P., and Doll, R.: Investigation of Relation Between Use of Oral Contraceptives and Thromboembolic Disease. A Further Report, Brit. Med. J. *2*:651-657 (June 14) 1969. **4.** Sartwell, P. E., Masi, A. T., Arthes, F. G., Greene, G. R., and Smith, H. E.: Thromboembolism and Oral Contraceptives. An Epidemiologic Case-Control Study, Amer. J. Epidem. *90*:365-380 (Nov.) 1969.

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Indication – Enovid-E is indicated for oral contraception.

The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

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Editorials

Supplements to Minnesota Medicine
The Kinsella Supplement

With this issue, subscribers to Minnesota Medicine receive as a supplement, Kinsella's "History of Thoracic Surgery in the Upper Midwest." The Board of Editors from now on will occasionally accept for publication as a supplement manuscripts which are of interest to its readers, but cannot be included in the regular columns of the journal usually because they are too long. Supplements will not be a frequent feature of the publication and will occasionally appear perhaps once or twice a year.

Minnesota Medicine thanks St. Mary's Hospital, its staff, and friends who have supported this Kinsella supplement.

Tom Kinsella, in the upper Midwest, essentially created the field of thoracic surgery. He started out, however, probably with no intention of making a career out of surgery. He had a general internship at the Minneapolis General Hospital (Hennepin County General Hospital) from 1919-1920. His fellowship at the Mayo Clinic from September, 1920 to January, 1922 was in the field of internal medicine.* Immediately thereafter we find him in the Nicollet Clinic as assistant in surgery.

Training for one specialty and practicing another is unusual but well known in medicine and there are some brilliant examples: E. T. Bell who was formally trained as an anatomist and Cecil Watson whose Ph.D. was granted under Bell in pathology.

Undoubtedly Kinsella's bout with pulmonary tuberculosis was crucial in his decision to make this disease his principal interest. In a letter his widow, Sally Kinsella, writes: "He left the Mayo Foundation January 1, 1922. He was assistant in surgery at the Nicollet Clinic in Minneapolis for one year. That is when he broke down with T.B., and became associate physician at Cragmoor Sanitorium, Colorado Springs, Colorado until July 1, 1925." Apparently T. J. Kinsella was not only a patient with pulmonary tuberculosis at Cragmoor, but also a physician on the staff. His primary achievements in thoracic surgery, particularly in pulmonary tuberculosis are recounted in Cohen and Priest's forward to the Kinsella supplement.

A delightful interlude in my junior year in medical school was a month spent at Glen Lake Sanatorium, on the service of Tom Kinsella. That was in the early thirties and by then he was famous for his successful thoracoplasties. Patients pleaded to be accepted for surgery by him knowing this was the surest way to be released from the Sanatorium. In his examining chamber however he was an internist, paying full attention to the history and carefully going over every possible physical finding with his students. He was always first a physician.

Dr. Kinsella enjoyed a unique reputation, expert in the medical care and diagnosis of chest disease and peerless in their surgical relief.

Reuben Berman, M.D.
Editor

*Terrace Topics, January, Vol. 1, No. 5 published by the Trudeau Club, Oak Terrace, Minnesota in 1934.

Doctor Thomas Kinsella

The History of Thoracic Surgery

Dr. Thomas Kinsella in his history which is published in the enclosed supplement lists many familiar men of medicine: Mixter, Plummer, Vinson, Rontgen, Wilms, Halsted, Estlander, Friedlander, Morgagni, Laennec, Virchow, Ochsner, Sippy, Kussmall, Billroth, Mikulicz, Blalock, Vineberg, Cushing, Dupuytren, C. H. Mayo, W. J. Mayo, and Nakayama. Surgical procedures, many unfamiliar, are included namely pneumonolysis, ligation of the pulmonary artery, therapeutic pneumothorax, surgery on the phrenic nerve, scalenectomy, and thoracoplasty.

There are accounts of interesting and fascinating cases, such as the one in June of 1898 when Dr. Eitel and Dr. Dunsmoor surgically removed a partial dental plate which had been impacted in the esophagus for six years.

The history is thorough. It takes the reader from the dawn of chest surgery to the most modern of advances, including transplant surgery. Interesting to note is that the heart pump goes back to at least 1928, and that experimentation with heart transplants goes back to 1931.

Many doctors, I suspect, feel that the world too soon forgets the accomplishments of its doctors, and a written history provides a way so that many can live a little longer. I am sure that Dr. Kinsella would have considered this a very weak argument, as this was not one of his motivating factors.

Those of us who had the opportunity of participating with Dr. Thomas Kinsella in the care of patients often felt the best part of all was the good doctor himself. Once again, the best part of his history is the personality of Tom Kinsella, himself.

Something of his whimsy is evident as he relates how Xray was demonstrated at the Minnesota State Fair in 1902, by Dr. A. A. Deslaurier, who was then a sophomore medical student and who had received the machine as a present from his father. You see the author as a detective ferreting out these many facts in order to credit the various advances to the proper people.

If the best part of the history is the author himself, then the best part of Dr. Kinsella was his feeling for his patients. You are left with the lasting impression after reading the history that Dr. Kinsella cared about people while he was caring for them.

Perhaps this is the greatest legacy a man can leave behind . . . his great love for people and his desire to make them well.

Milton H. Seifert, M.D.
Excelsior, Minnesota

Familial Idiopathic Hypoparathyroidism

Doctors Olin and Poindexter* report direct attention to two points of practical clinical importance. The first is the necessity of physicians being aware that failure of one endocrine gland may herald the onset of failure of others. Further, the discovery of a patient with endocrine deficiency is indication for a careful review of families for other similarly affected members.

The second point reminds physicians that antibodies against endocrine glands may be present long before clinical and laboratory evidences of specific glandular failures are manifest. Although the presence of antibodies against a clinically unaffected gland undoubtedly has significance, it is not certain that all such patients will develop failure of all of the glands but surveilance for their possible failure is indicated.

A. B. Hayles, M.D.
Rochester, Minnesota

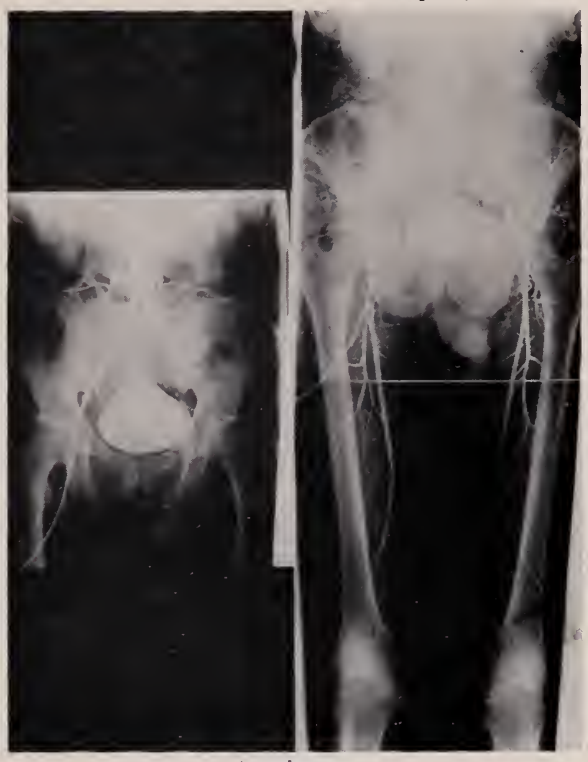
*See page 701.

Aorto-Iliac Disease—Small Arteries Syndrome

THE CLINICAL PROBLEM of occlusive disease of the aorto-iliac arterial system is presented by Rockwell.* The diagnostic work-up and treatment has become quite standard and is available in most major hospitals in Minnesota. The management of these patients must be individualized to a high degree due to the wide variations in the extent and location of the occlusive disease. A small number of patients presenting with aorto-iliac occlusive disease will be found to have "small artery syndrome." In this situation the aorto-iliac system (in addition to the entire arterial system) is smaller than in most individuals. Indeed, the transverse diameter of the abdominal aorta often runs 30% to 50% of normal. The accompanying arteriogram represents the aorto-iliac system of a 170 pound six foot male with an abdominal aorta measuring under one and one-half centimeters in transverse diameter. In individuals with "small arteries" the build up of atheromatous debris within the lumen leads to symptoms and findings of limb ischemia earlier than in patients with normal sized arteries. The principles of treatment, however, remain the same in all cases, namely to restore pressure and flow to the groin.

*Rockwell, E. G.: Aorto-Iliac Disease. Minnesota Med 55:5:430, 1972.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota



Arteriogram

Treatment of Bone Tumors in Children

DR. COVENTRY* has made a concise summary of the treatment of the most common bone tumors found in children. Much useful information also is included in regard to diagnosing these lesions.

The most important differential point is whether the lesion is benign or malignant and except for some of the more common and characteristic x-ray appearances biopsy is required to make this differentiation.

Survival rates in series of patients with osteogenic sarcoma and Ewing's sarcoma remain somewhat controversial. The 20 percent five-year and 17 percent 10-year survival quoted in this article is higher than the range of survival reported by most series. Some other series have reported five-year survival as five percent or less.

Osteogenic sarcoma and Ewing's sarcoma, the most malignant of the children's bone tumors fortunately are relatively rare. It is difficult to recall, however, a patient with either of these conditions who has survived even five years despite prompt diagnosis and amputation treatment. Nonetheless, to quote Dr. Dahlin, the relatively favorable data reported here "should help dispell the notion that the prognosis of osteogenic sarcoma is so poor that prompt and proper therapy is useless."

*Coventry, Mark B.: Treatment of Bone Tumors in Children. Minnesota Med 55:6:536, 1972.

Joseph M. Tambornino, M.D.
Minneapolis, Minnesota

Teaching Medicine in Private Hospitals

MEDICAL EDUCATION in the undergraduate days of most of the readers of MINNESOTA MEDICINE was rather rigidly separated into basic sciences the first two years and clinical studies the Junior and Senior years. The junior year at Minnesota consisted of amphitheatric lectures by the professor to a seated class with perhaps one in a hundred called down to inspect, palpate, or auscultate. The house staff made rounds with attending and consulting professors taking notes of their suggestions (which really were orders) and following hierarchial protocol. That's how it used to be, but things are different now. Theologides* elsewhere in this issue discusses the curricular change and really revolutionary transformation in the medical school. The attitudes of medical students and student doctors have changed with profound effect upon academic teachers.

Now students in the freshman year are involved in clinical exercises. The old devil of the junior year shuttling students from Eustis to Todd Amphitheater is no more. Juniors are working in hospital wards, and Seniors are writing orders like interns. They are interns in every respect except nowadays they go home nights (most nights). One can predict the early demise of the traditional intern year.

The ferment among students affects not only those in academic medicine. The University of Minnesota accepted 227 entering freshmen medical students in 1971. This represents nearly double the number of a decade ago. Private hospitals are asked to share in the clinical training of these students and, indeed, already in Twin Cities hospitals are found phase B sophomores and junior and senior interns learning in small groups with "compassionate and expert physicians" as described by Theologides. With the new medical schools opening in Duluth and Rochester this year, clinical teaching in the communities will be done exclusively in private hospitals. In the private hospital the students can study patients not already violated by too numerous examinations. They learn. They also teach by asking difficult questions of the tutor.

It is possible also for the new breed of house staff to practice in the medical wards of private hospitals. The admitting physician discusses the diagnostic and therapeutic problems, listens to the house staff recommendations, and may suggest other studies, consultation, and therapy which will be actually written down as orders by the intern. This is not an easy role for the physician who admits (owns) the patient. It requires extraordinary restraint on the part of the senior staff and considerable understanding on the part of the house staff of the responsibilities of the patient's physician which are not abdicated by assigning the patient to a teaching service.

We are in a new era of medical education, not only within the university, but deeply involving private hospitals also. What Theologides has to say about academic internists applies also to an increasing number of non-academic internists and family practitioners who are involved in the clinical teaching of medical students. Physicians all over the state including such towns as Cloquet, Austin, Hibbing, and Montgomery have medical students living in their towns learning medicine at the "grass roots" level, so to speak. Right now, 23 such medical students are on this program. The end result of these programs extending undergraduate medical education to private hospitals and into family practitioners' offices must be better care of the patient.

Reuben Berman, M.D.
Minneapolis, Minnesota

*See page 743.

Meeting

The 32nd Annual AMA Congress on Occupational Health will be held at The Drake Hotel in Chicago, September 11-12, 1972. Contact Dr. Henry F. Howe, AMA, 535 North Dearborn Street, Chicago for further information and reservations.

Temporal Lobe Seizures

)R. RUSSELL B. BUTLER* presents an interesting view of temporal lobe seizures with emphasis n historical perspective and their anatomic substrate. Some points he raises would seem to arrant further comment.

Automatisms associated with temporal lobe izures may be clinically indistinguishable from ose occurring with associated generalized spike id wave discharges in the electroencephalogram, r from automatisms occurring after a generalized nic-clonic seizure. This lack of specificity of inically observed episodes may indicate that they sult from a release phenomenon rather than om a specific epileptic discharge through obcure motor pathways. It may be that when, as result of electrographic seizure discharge or ostictal suppression, critical areas of the brain re functionally disconnected from certain other reas, the latter areas are "released" and an automtism occurs. The association of the psychic henomena reviewed by Dr. Butler and the elecoencephalogram makes clinical differentiation asy in most cases.

Although it is true that some patients with temoral lobe seizures have disorders of personality r emotion or both, some careful studies measurng various parameters of psychologic and emoonal status have not shown consistent differences etween temporal lobe patients as a group and ther epileptics or nonepileptics. It is often almost mpossible to assess the cause of psychopathology in the individual patient with temporal lobe epilepsy. The disturbance may be an ictal or postictal phenomenon; it may be the result of anticonvulsant medications or the result of the same cerebral pathology that caused the convulsive disorder; or it may be a reactive emotional disturbance. Any or all of these factors may be acting at various times in a given person.

The rationale for prescribing primidone and phenobarbital concurrently is obscure. It is well established that the metabolism of primidone is considerably more complex than that of phenobarbital. The bulk of orally administered phenobarbital is excreted, unchanged, by the kidneys. Primidone is partially metabolized as phenobarbital (10 to 25%); but in addition, primidone itself and another of its major metabolites, phenylethylmalonamide (PEMA), have been shown to have anticonvulsant properties in experimental animals. Primidone therapy therefore has the theoretical advantage over phenobarbital therapy of giving these two additional anticonvulsants. For a given blood level of phenobarbital, higher levels of the other two (primidone and PEMA) can be achieved if primidone is prescribed alone. Despite its theoretical advantages, controlled crossover trials in epileptic patients have shown that primidone therapy is no more effective than phenobarbital therapy when the doses of each are such that blood levels of phenobarbital are kept constant.

William E. Karnes, M.D.
Rochester, Minnesota

*See page 755.

Intussusception in Infants and Children

THE TREATMENT of intussusception has swung ike a pendulum between medical and surgical xtremes.

Prior to 1871, no successful operation had been erformed and the disease was almost always atal. In 1876 Hirschsprung of Copenhagen pubished his first report on the use of a hydrostatic ressure enema. His results were superior to any urgical series for nearly 70 years with a mortality of about 35 percent in contrast to the surgical mortality at that time of 80 percent.

After 1940 the pendulum swung to surgical therapy as improved technique, better anesthesia, and antibiotics helped to reduce the mortality well below that achieved by enemas alone. The barium enema in the next two decades was used primarily as a diagnostic tool with little attempt to reduce the intussusception.

Beginning about 1960 and continuing to the present time the pendulum has come to rest near the center. At the prodding of men like Ravitch, most surgeons now agree that a contrast hydrostatic enema under careful control, augmented by surgery when required, represents the best treatment of this disease. The thoughtful report by Thomas in the July issue is in agreement with this view.*

Still unanswered are several clinical observations which have intrigued me for many years concerning infants and children. Why does intussusception tend to occur in sturdy, well nourished "butter-balls" rather than in malnourished infants? Why are there seasonal peaks in the incidenc does it relate to adenovirus infection? Why th strong preponderance in males? Why does th disease peak between five to ten months of ag and sharply decline after a year? And, one fin perplexing question, why should there be a strikin variation in the incidence of intussusception in di ferent regions of the world? The British Isles an Scandanavia see a markedly higher incidence tha the United States. In this country we have regularl seen more cases in Minneapolis each year tha are reported from large centers in Baltimore, Ne Orleans and New York, indicating a definite r gional variation in the incidence.

*Thomas, John: Intussusception: Revisited. Minnesota Med 55:627, 1972.

Bernard J. Spencer, M.I
Minneapolis, Minneso

Intramuscular Neurolysis for the Relief of Spasticity

INTRAMUSCULAR NEUROLYSIS as an adjunct in the treatment of spasticity, discussed by Awad in this issue,* has received scanty attention in the literature, probably because it is not being practiced widely.

At the Mayo Clinic, we began using phenol blocks of motor points of skeletal muscle in spastic patients four years ago and have employed this therapy in cases of multiple sclerosis, stroke, traumatic myelopathy, and cerebral palsy. The technique is mastered readily, especially by those with a background in clinical electromyography and, as noted by Awad, has proved to be free of significant local irritative and systemic toxic side-effects.

Our experience with intramuscular phenol blocks has varied. With few exceptions we have failed to provide relief in patients with myelopathy in whom the objective was to reduce massive flexor or extensor spasms of the lower extremities. We no longer treat this type of problem with chemical neurolysis. Better results have been attained when the aim was to reduce adductor or hamstring muscle spasticity or to lessen foot clonus that interfered with ambulation. The most satisfy ing results have followed treatment directed a highly selected muscle groups as in loosening a tightly folded thumb, opening a clawed hand, o reducing inverter or flexor spasticity of the foot Given a limited permissible amount of phenol pe treatment session, it is simpler to accomplisl clinically effective neurolysis when functional im provement depends on alleviation of spasticity i a single muscle or muscle group than in multipl muscle groups. Furthermore, some extremit muscles are located easier technically with th probing needle than are others.

Our initial enthusiasm for phenol blocks o motor points in the treatment of spasticity ha waned somewhat and we now confine this mod of therapy to highly selected patients. We hav not had experience with the use of phenol neurol ysis of peripheral nerve trunks, as advocated b Khalili and others, but have wondered whether th overall results may not be superior to and th procedure less time-consuming than the use o muscle motor point blocks.

Juergen E. Thomas, M.D
Robert R. Sawtell, M.D
Rochester, Minnesot

*See page 711.

Special Article

The Internist in Academic Medicine

ATHANASIOS THEOLOGIDES, M.D., Ph.D., F.A.C.P.

IN ALMOST ALL departments of medicine major changes have taken place in the medical curriculum, in the training for specialization, in the emphasis on research and in the interest and involvement in primary health care of the community. These changes affect the specialty of internal medicine and particularly the internist in academic medicine. There is a need for re-evaluation of his function as a clinician, teacher, and investigator.

In the last decade, there has been a remarkable change in the attitudes of the medical student toward learning. The student is no longer satisfied with a passive accumulation of information geared mainly to pass examinations and to score high on tests. He is interested in a medical curriculum relevant to the demands of the practice of medicine with an early and frequent contact with patients. He wants to master the process of learning medicine and of maturing clinically through an active participation in the planned teaching and through independent projects on free time.

These changes resulted in a shift of undergraduate medical teaching from the formal amphitheater lecture to bedside instruction and dialectic sessions in small groups. The academic internist is required to have significant competence in bedside clinical medicine. As a clinician with a good working knowledge in all areas of internal medicine coupled with a compassion for the patient he can initiate and guide the student in the establishment of rapport with the patient, in the procurement and analysis of clinical and laboratory data, their evaluation and synthesis for diagnosis, and finally in the process of management and therapy.

During the same period the philosophy of learning of the house staff has significantly changed. The house staff has developed the attitude of learning clinical medicine by assuming complete control of the diagnostic and the therapeutic management of the patient. Instead of proceeding under a close supervision and guidance by a faculty member they prefer to carry on the work-up and therapy independently and to call various faculty members to consult only on specific questions in their own subspecialty.

There is no doubt that today's intern and resident are better prepared, more mature clinically, and have more free time to look in the medical literature for help on diagnostic and therapeutic questions. However, it would be precarious to accept the resident as a seasoned internist capable of managing the patient without close supervision. Active guidance still represents an important aspect of the clinical training and the only way for the young physician to have the benefits of the experience of the mature clinician. But to exercise meaningful clinical supervision, the responsible faculty member has to gain the respect of the house staff for his knowledge, competence, and his ability to handle any problem in internal medicine at large. Expertness only in a limited area is not an adequate qualification for the role of the attending physician.

With a changing student, intern and resident there is a changing patient population in the teaching hospital. The increasing number of well-trained physicians and competent consultant-specialists in the community has decreased the need for the patient referral to the teaching hospital for the diagnosis and the management of the rare and complicated syndrome. On the other hand the proliferation of commercial laboratories for the unusual test has abolished the monopoly of a few investigators in teaching hospitals for the special test or the determination of a certain metabolite crucial for the diagnosis of a certain disease. The patient population of the teaching hospital resembles more and more the population of any private hospital with the exception of a greater number of patients with incurable diseases. Moreover, with the involvement of departments of medicine in primary health care the clinical teaching has to be done more and more on patients with conditions and diseases seen in

Dr. Theologides is an Associate Professor of Medicine, University of Minnesota Hospitals, Minneapolis, Minnesota.
See editorial, page 740.

the practice of medicine in the community and not on the patient with the rare syndrome.

All these changes emphasize the need in academic medicine of the well rounded internist with knowledge and clinical competence in all areas of internal medicine and not the narrow subspecialist with depth and research accomplishments only in a very limited region. The academic internist should be primarily an excellent clinician but who also has interest and competence in teaching and research.

The young physician who plans a career in academic medicine should have an intensive and broad training during residency and fellowship years and also frequent formal periodic retraining throughout his career in areas of internal medicine outside his own subspeciality. An area especially that should be emphasized is his education in the technique of teaching. It has been assumed that a good clinician is also a good teacher; but very often this is not the case. Therefore, instructions in teaching methods should be an added element in the training of the internist for academic medicine and periodic evaluation of his competence as a teacher should be stressed. During the formative years some administrative duties should be assigned to him for experience in problems and decision making in administration. Cours in personnel management would add a stron component to this experience.

Besides growing to be a competent clinician an teacher the young academic internist should als work to develop as an investigator. He shoul participate and later conduct independently clin cal, epidemiological or experimental research i an effort to find answers to bedside question In addition to contributing to the understandin and treatment of diseases, he can evaluate the re search contributions of basic research scientis and their applications to clinical medicine. B raising questions and trying to find answers he ca maintain an open inquiring mind to soften th absolutism of the pedagogue.

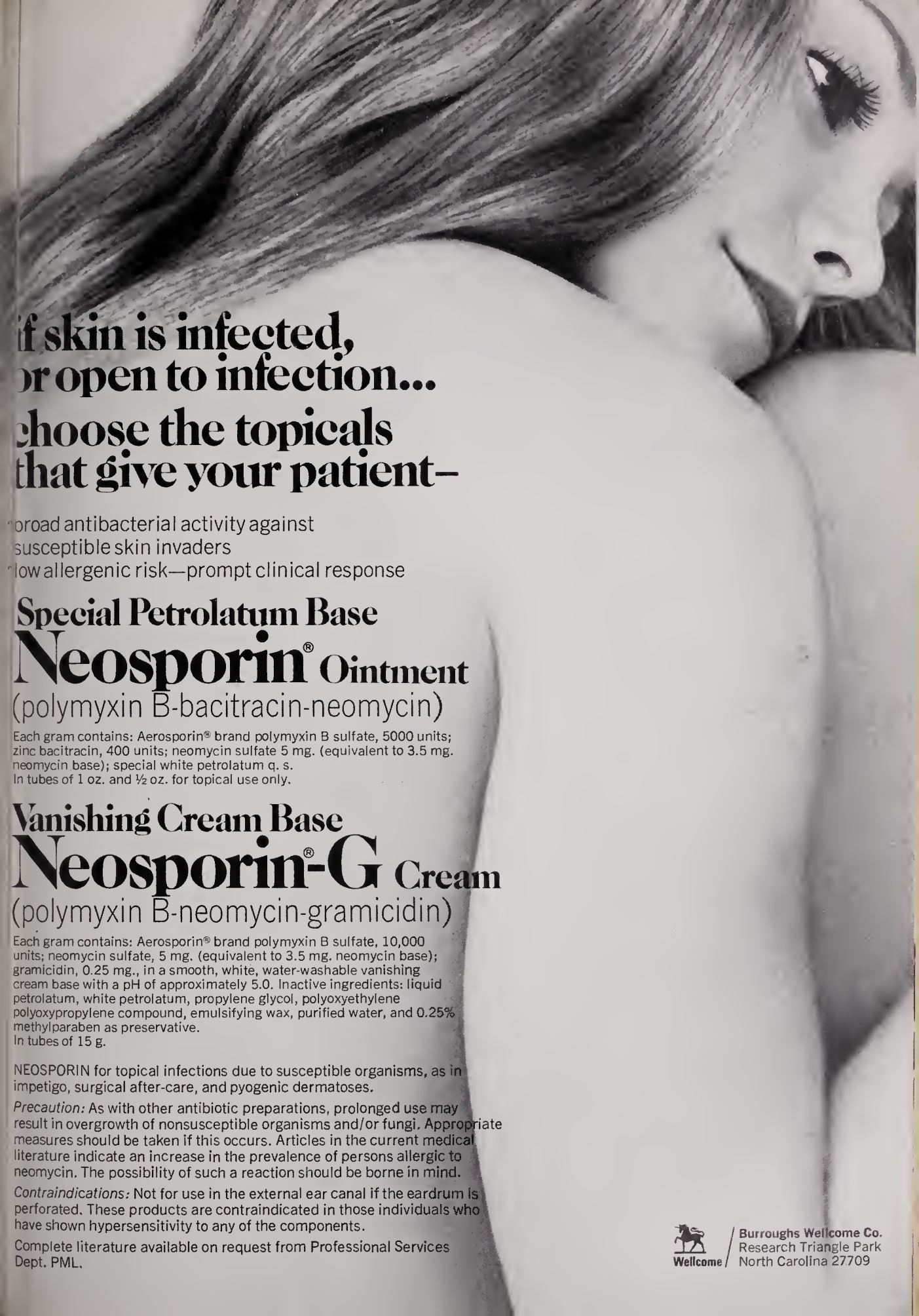
It appears therefore that with the changin world of patient care, student teaching, physicia training, and the need for more applied research the training programs for the development c academic internists should be re-evaluated. I these programs the new scientific and professiona requirements should be interwoven with the che ished old personal, cultural and social values c gentleness of feeling, concern and compassion fo the sick and the desirability of social commitmen

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Psychiatry

I moved my lips—the Pilot shrieked
And fell down in a fit;
The holy Hermit raised his eyes,
And prayed where he did sit.
I took the oars: the Pilot's boy,
Who now doth crazy go,
Laughed loud and long, and all the while
His eyes went to and fro.
"Ha! ha!" quoth he, "full plain I see,
The Devil knows how to row."*

*Samuel Taylor Coleridge, "The Rime of the Ancient Mariner."



If skin is infected, or open to infection...

choose the topicals that give your patient–

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

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(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
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NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

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When you select this familiar antibiotic for IV infusion you have available a broad dosage rang that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomyc hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water But when 4 grams or more per day is given, Lincocin should be diluted in n less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25—30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency trea e. *Skin and mucous membranes*—Skin he urticaria, vaginitis, and rare instances e foliative and vesiculobullous dermatit a been reported. *Liver*—Although no dir re lationship to liver dysfunction is estab he jaundice and abnormal liver functio es (particularly serum transaminase) hav ec observed in a few instances. *Cardiov* —Instances of hypotension following re teral administration have been rep e particularly after too rapid IV admi tr tion. Rare instances of cardiopulmon a rest have been reported after too ra l administration. If 4.0 grams or more a ni istered IV, dilute in 500 ml of flui ar administer no faster than 100 ml per *Special senses*—Tinnitus and vertigo av been reported occasionally. *Local rea* —Excellent local tolerance demonstra intramuscularly administered Lin c (lincomycin hydrochloride). Reports o pa following injection have been infre e Intravenous administration of Linco 250 to 500 ml of 5% glucose in d water or normal saline has produc n local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *5* Capsules—bottles of 24 and 100. *Solution, 300 mg per ml*—2 and 10 m and 2 ml syringe. *Syrup, 250 mg pe* —60 ml and pint bottles.

For additional product information, s the package insert or see your U h representative.

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Upj n

Violent Death and Alcohol Use

Among the Chippewa in Minnesota

JOSEPH WESTERMEYER, M.D., Ph.D. and JOHN BRANTNER, Ph.D.

N DOING CLINICAL work with Chippewa patients, stories of multiple traumatic events are com- only obtained. Moreover, in taking family his- ories with these patients, violent deaths appear to frequent. For example, among the first degree latives of thirty Chippewa alcoholics, 23 out of deaths (28.4%) occurred by accidents, homi- de, or suicide.

The literature demonstrates a high association etween violent death and alcohol use. Postmor- m examinations, done on single vehicle accidents New York, demonstrate that two-thirds of the talities have blood alcohol above 0.05%.[1] mong car accident casualties in New Zealand, ixty percent have blood alcohol of 0.10% or igher.[2] Using the case study method, over a hird of fatal accidents have been shown to in- olve chronic alcoholics.[3] Other violence also ears a strong relation to alcohol, as demonstrated y breathylyzer tests on victims of fights, assaults, nd home accidents in a Boston emergency room.[4]

Violent death may be common among Chip- ewa people. Among other groups of people iolent injuries or death are frequently associated with alcohol usage. We were therefore interested o see first, whether violent death is common mong Chippewa; second, whether violent death s associated with alcohol use among Chippewa; nd third, how the epidemiology of violent death mong Chippewa differs from the general popu- ation and other Indian groups.

Department of Psychiatry, University of Minnesota.

Method

Vital statistics for the state of Minnesota include "Indian" as a racial category. In the 1960 census, 95.4% of Minnesota Indians were estimated to be Chippewa. Thus, the category "Indian" in Minnesota virtually means Chippewa people.

Postmortem investigations are performed for all cases of violent death by the Hennepin County Medical Examiner. Investigation includes chart review, autopsy, police report, and—where indicated—analysis of blood or gastric contents for alcohol. Again, "Indian" is a racial category in these data. Based on information from the American Indian Employment Center in Minneapolis, between 80 and 90% of Indians in the area are Chippewa. As a result, detailed autopsies are available for those Chippewa people who die in the Minneapolis area.

Methodologically, data from urban Chippewa must be cautiously applied to the state-wide Chippewa population. Supportive information suggests that such a generalization can be reasonably made.

Data

Minnesota Vital Statistics

Violent Death Among Minnesota Indians. Violent deaths comprise the most common form of death among Minnesota Indian people during 1965-67 (Table 1). While one out of four Indian people die by such causes, only one out of twenty occurs in the general population. This category ranks fourth in the general Minnesota popu-

TABLE 1
Major Causes of Death
State of Minnesota
1965 - 1967

Cause of Death	Indian People					
	Rank	Number	% of all deaths	Rank	Number	% of all deaths
Accidents, violence	1	120	25.8%	4	5,205	5.3%
Heart disease	2	105	22.6%	1	37,666	38.2%
Pneumonia, influenze	3	40	8.6%	6	2,826	2.9%
Dis. Digestive System	4	36	7.7%	5	3,303	3.3%
Cancer	5	34	7.3%	2	17,107	17.4%
Stroke	6	23	4.9%	3	13,294	13.5%
Other	—	107	23.0%	—	19,208	19.5%
Total		465	99.9%		98,609	100.1%

lation. Despite the relatively small number of Indians, the differences are highly significant ($P < .005$).

Hennepin County Medical Examiner

Violent Deaths, Hennepin County. During the years 1964-69 inclusive, 3305 violent deaths came to the attention of the medical examiner. Of these 41 (1.24%) were tabulated as Indian. Table 2 indicates the individual numbers for non-vehicular accident, vehicular accident, homicide, and suicide.

TABLE 2
Violent Deaths
Hennepin County Medical Examiner
1964 - 69

		Indian Deaths	
Cause of Death	Total Number of Deaths	Number	Percent of Total
Non-vehicular accident	1411	21	1.49%
Vehicular accident	1047	11	1.05%
Homicide	229	7	3.06%
Suicide	618	2	0.32%
Total	3305	41	1.24%

Non-vehicular Accidental Deaths. Of 21 Indian cases, 15 were judged to be alcohol related based on the medical investigation. Ages for all alcohol related deaths ranged from midteens to midfifties, while deaths not related to alcohol occurred in infancy or after the late fifties. Alcohol related causes of death included: falling (seven people), acute alcohol intoxication (three), carbon monoxide poisoning (three), and drowning (two).

A comparison was made between the Indian deaths (1964-69) and "all" deaths in 1969 (Table 3). A marked difference in mean age is not duc to the greater proportion of elderly peo in the "all" sample. By excluding all perso age 70 or older, the adjusted mean ages so c tained are similar. Sex ratios for both grou are similar.

Of those blood alcohol tests having positi results, the mean level of Indian tests is high than the "all" tests. Contributing to this diff ence are several cases of non-Indian people dyi of intoxication from alcohol plus other dru (barbiturates, amphetamines, analgesics). Into cation deaths among Indian people involve alcoh only.

Vehicular Accidental Deaths. Seven of t eleven Indian deaths were judged as alcoh related. In comparing Indian and "all" deat for age, sex, and blood alcohol, differences b tween the two groups are not significant.

Homicide Deaths. Of the seven homicide vi tims, four had elevated blood alcohol at the tir of death. Comparisons for age and sex do n demonstrate significant differences between t two groups. However an age disparity may b present: mean Indian age falls two decades behi the general population. Despite the few India in the sample, statistical testing for age do demonstrate a significant difference at the .0 level of probability (Table 4).

Suicide Deaths. One of the two Indian suicid was alcohol related. With so few Indian suicid

TABLE 3
Characteristics of Violent Death
Hennepin County Medical Examiner

Category	Indian deaths (1964-69)	All deaths (1969 only)
Non-auto accidents		
Number	21	297
Mean age	37.5 years	53.4 years
(Adjusted age)	(35.2 years)	(34.9 years)
Percent males	62%	63%
Mean blood alcohol (pos. tests only)	0.267%	0.207%
Auto accidents		
Number	11	163
Mean age	38.1 years	36.6 years
Percent males	73%	67%
Mean blood alcohol (pos. tests only)	0.175%	0.176%
Homicide		
Number	7	40
Mean age	18.3 years	38.7 years
Percent males	86%	77%
Mean blood alcohol	0.155%	0.177%
Suicide		
Number	2	101

vailable for scrutiny, comparisons are meaningss. However the paucity of suicides is itself a gnificant finding worthy of further attention.

TABLE 4
Comparison of Homicide Victims by Age
Hennepin County Medical Examiner

Age Group	Indian deaths (1964-69)	All deaths (1969 only
ess than or equal to 25 years	7	12
ver 25 years	0	28

Fisher Exact $X^2_1 = 14.3, <P .005$

Blood Alcohol Tests. Blood alcohol tests offer fairly objective standard for comparison between ie two groups. Since the number in any one ubcategory of violent death is small, there is alue in grouping them together. As noted in able 1, the relative proportion of Indians to ie general population varies for each category. Iowever, the two largest categories, vehicular and onvehicular accidents, do not vary as widely as o the two smaller categories, homicides and uicide.

Blood specimen for alcohol content tend not o be taken from the very young or the very old. Among those who survive a long time posttrauma, in autopsy alcohol specimen is of no value. So lood alcohol specimens are reserved for persons vho may have recently taken alcohol. Comparing he Indian and "all" groups in Table 5, signifiantly more specimens have been taken from ndian persons at autopsy (at $P < .025$). Table 5 demonstrates that significantly more Indians have positive blood alcohol tests at autopsy relative to the general population ($P < .005$).

Discussion

Incidence of violent death among the Indian people of Minnesota is five times that of the general population. Based on data from Minneapolis, Indian violent death appears to be associated with alcohol to a significantly greater extent than in the general population.

TABLE 5
Comparison for Taking Blood Alcohol Specimens
Hennepin County Medical Examiner

Category	Indian deaths (1964-69)	All deaths (1969 only)
Specimen taken	26	269
Specimen not taken	15	331

$X^2_1 = 5.23, \ P < .025$

Despite these disparities between the two groups, notable similarities occur as well. Proportion of males and females does not vary significantly between Indians and the general population. Mean blood alcohol levels, taken from positive tests only, compare closely. Difference in mean alcohol level among nonvehicular accidental deaths appears related to the use of other drugs in the general population and the absence of such use among the Indian deaths.

Age distributions coincide only for the vehicular accident category. However, if persons aged 70 or older are excluded from nonvehicular accidents (few Indian people survive that long), then the two groups also compare closely for age. Only among homicide victims does there appear to be a significant age discrepancy, with Indian victims being significantly younger. Of interest here also is the relatively high rate of homicide victims in the Indian group.

These observations, the young age and high rate of Indian homicide victims in Minnesota, have been noted for Indian people in general in the United States.[5] Thus, the Minnesota Indian population, while unlike other Minnesotans in these regards, resembles other Indian people.

Minnesota Indian people appear to differ regarding suicide, however. Nationwide Indian statistics,[5] as well as work done by Dizmang and Resnick among tribal groups,[6-8] indicates quite a high rate of Indian suicide. One might wonder whether Indian suicide data from an urban area such as Minneapolis might be misleading or whether Chippewa people actually have less suicide.

Paredes[9] collected vital statistics from northern Minnesota, including Beltrami and Cass Counties where Chippewa reservations are located. His records cover 20 years (1940-64) and include homicide and suicide figures by race. Using the 1960 population for Cass and Beltrami Counties, the following crude homicide rates are obtained: 7.0 per 100,000 Indians per year, versus 1.3 per

TABLE 6
Comparison for Results of Blood Alcohol Specimens
Hennepin County Medical Examiner

Category	Indian deaths (1964-69)	All deaths (1969 only)
Alcohol present	23	118
No alcohol	3	151

$X^2_1 = 18.94, \ P < .005$

100,000 non-Indians per year. Again using the 1960 population as a denominator, crude suicide rates are: 6.1 per 100,000 Indians per year, and 10.7 per 100,000 non-Indians per year. Thus, for reservation areas, Chippewa homicide is much higher and Chippewa suicide is somewhat lower as compared to the general population. These rural data coincide with the urban statistics, both indicating a relatively low rate of Chippewa suicide and a relatively high rate of Chippewa homicide.

These differences in suicide rates among Minnesota Indians (mostly Chippewa) as compared to other Indian groups underscore an important point. While it is proper to look for trends and similarities among ethnic groups, it is an error in logic to assume conditions prevalent among one Indian tribal group will be present among another tribal group. The exceptions to general rules may provide clues.

There are no satisfactory explanations for the low rate of Chippewa suicides relative to the general Minnesota population and relative to other Indian groups. In fact prior clinical experience would have suggested a high rate. For example, 10 out of a series of 30 Chippewa alcoholics admitted to at least one suicide attempt, and several more reported suicidal preoccupation. In the last year at our institution, three Chippewa girls have gestured suicide by scratching or cutting their wrists during hospitalization. While one might logically argue that the "plea-for-help" gesture might inveigh against actual completed suicide among the Chippewa, we have no other data to support this contention.

The question inevitably arises: Why so mu violent death among Minnesota Indians? In ad tion the exact nature of the alcohol-violence rel tionship is not clear. Is there more alcoholis among Indians in Minnesota? Do alcohol u and violence-seeking comprise a form of suicid or perhaps function as a depressive equivalen Or does risk-taking combined with alcohol u function as a mode of obtaining prestige? (relieving boredom?

Conclusions

Violent death occurs five times more oft among Indian people in Minnesota (most of who are Chippewa) than among the general popul tion. It is the most common cause of death f Indians in Minnesota during recent years.

In Minneapolis, violent deaths among India are significantly more often associated with alcoh use than in the general population.

In general, Chippewa victims of violent dea resemble such victims in the general populati with regard to sex, age, and blood alcohol lev A notable exception to this is homicide, whic occurs at an earlier age among Chippewa (as does among other American Indians). Homici occurs particularly often among Chippew whereas, unlike other Indian groups, suicide not so frequent.

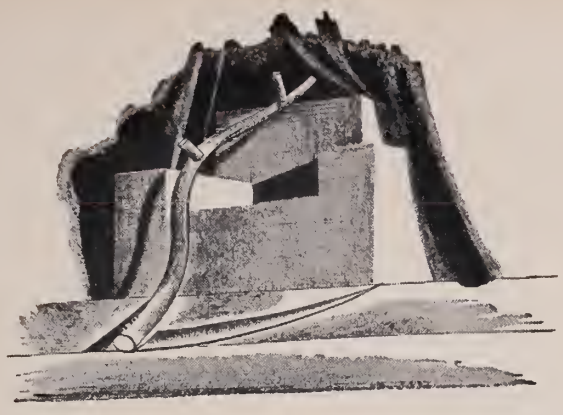
Acknowledgement

Appreciation is expressed to Dr. Sidney Finklestein a Mr. Robert Hiller of the Minnesota State Department Health, Dr. John Coe of the Hennepin County Exam ner's Office, and Dr. Jacob Bearman of the Departme of Biometry at the University of Minnesota.

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Strange how much you've got to know, before you know how little you know.



In Memoriam

Death is the golden key that opens the palace of eternity—Milton

IVAN T. CLARK, M.D.

Dr. Ivan T. Clark, 64, Sun City, Arizona, formerly of Duluth, died June 30. Born in Edgar, Nebraska, he graduated from Ohio State Medical School in 1941. A veteran of World War II, Dr. Clark went to Duluth in 1945 and moved to Sun City in the fall of 1970.

He was Chief of Radiology and former Chief of Staff at St. Mary's Hospital. Dr. Clark was a member of the St. Louis County Medical Society, the American Medical Association, the Minnesota State Medical Association and the Maricopa County, Arizona, Medical Society. He was a diplomate of the American Board of Radiology.

Dr. Clark is survived by his wife, Rosemary and two daughters, Mrs. Douglas Farnham and Mrs. Thomas King.

HENRY E. MICHELSON, M.D.

Dr. Henry Michelson, 83, a dermatologist, died May 10. He instituted the Dermatology Clinic at Hennepin County General Hospital, was Head of Clinic Service of the Division of Dermatology at the University of Minnesota Medical School, Professor and Director of the Division, emeritus professor following retirement in 1957 and consultant at Veterans Hospital and in postgraduate teaching at the Continuation Study Center.

Dr. Michelson was an examiner on the American Board of Dermatology, president of the Society of Investigative Dermatology, member of the editorial board of the AMA *Archives of Dermatology* and served as an editorial adviser for *The Journal Lancet*. He received the Outstanding Achievement Award of the University of Minnesota.

He was also a member of the Hennepin County Medical Society and the American Medical Association and 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by a son, Robert, and a daughter, Mrs. Scotson Webbe.

JOHN F. BRIGGS, M.D.

Dr. John F. Briggs, 67, St. Paul internist, died May 10. A native of St. Paul, Dr. Briggs had practiced there since the early thirties.

He was a past president of many medical organizations, including the American College of Chest Physicians, Minnesota Heart Association, Minnesota Thoracic Society and the St. Paul Society of Internal Medicine. He was an authority on both heart and lung diseases and served on many international, national, state and local medical committees relating to these ailments.

Dr. Briggs was a long-time chairman of the Minnesota State Medical Association's Committee on Pulmonary Diseases and its Heart Committee and served for many years as Public Relations Chairman for the Ramsey County Medical Society.

He was born in St. Paul, attended the University of Minnesota Medical School and interned at the Ancker Hospital.

There are no survivors.

PERCY A. MATTISON, M.D.

Dr. Percy A. Mattison, 69, Winona Urologist, died December 28, 1971. Born in Gardiner, New York, Dr. Mattison obtained his medical education at the University of Colorado Medical School in Denver.

He was a member of the Winona County Medical Society and the American Medical Association and an Associate Member of the Minnesota State Medical Association.

Dr. Mattison is survived by his wife, Mary.

HYMAN S. LIPPMAN, M.D.

Dr. Hyman S. Lippman, 76, St. Paul psychiatrist, died April 17. A former director of the Wilder Child Guidance Clinic, Dr. Lippman assisted in the development of a division of child psychiatry at St. Paul Ramsey Hospital.

Born in Minneapolis and educated at the University of Minnesota Medical School, Dr. Lippman spent 18 months in Vienna studying child and adult psychiatry. He was a member of the Ramsey County Medical Society, the American Medical Association and a 50 Club member of the Minnesota State Medical Association.

He is survived by his wife, Adelaide.

EDWARD M. LITIN, M.D.

Dr. Edward Litin, 51, Chairman Emeritus of the Department of Psychiatry at the Mayo Clinic, and an Associate Professor of Psychiatry at the University of Minnesota Graduate School, died April 28. He was born in Minneapolis and received his education at the University of Minnesota.

Dr. Litin was a past president of the American Psychiatric Association, a member of the Zumbro Valley Medical Society and the American Medical Association and an Associate Member of the Minnesota State Medical Association.

He is survived by his wife, Lorraine, daughter Nancy Jo and a son, Scott, who is a medical student at Houston, Texas.

OWEN F. ROBBINS, M.D.

Dr. Owen F. Robbins, 65, a past chief of staff at St. Barnabas Hospital, died May 29. He was also a staff member of the Fairview-Southdale Hospital and a member of the American Board of Surgeons, Obstetricians and Gynecologists.

Dr. Robbins was a member of the Hennepin County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Marjorie, two daughters, Mrs. Harold Pohlad and Mrs. Jan Ebert, and a son, Dr. Thomas O. Robbins of Detroit.

ARTHUR E. WALKER, M.D.

Dr. Arthur E. Walker, 68, St. Paul physician, died May 27. Born in Duluth, Dr. Walker obtained his medical education at Marquette University.

He was on the staffs of both St. Joseph's and Miller Hospitals and a member of the Ramsey County Medical Society and the American Medical Association and an Associate Member of the Minnesota State Medical Association.

Dr. Walker is survived by his wife, Esther, and tv sons, Curtis and Stuart.

JOSEPH D. SELMO, M.D.

Dr. Joseph D. Selmo, 61, Norwood surgeon, died M 11. He was born in Baltic, Michigan, and obtained h medical education at Loyola University School of Me cine in Chicago.

He was a member of the McLeod County Medic Society, the American Medical Association and t Minnesota State Medical Association.

Dr. Selmo is survived by his wife, Ruth.

MARVIN J. GEIB, M.D.

Dr. Marvin J. Geib, 59, Chief of Staff at St. Ansg Hospital in Fargo, died July 6. He was a founder of t Neuropsychiatric Institute in Fargo.

Born in Gaylord, Minnesota, Dr. Geib graduated fro the University of Minnesota Medical School in 193 He was a member of the Clay-Becker County Medic Society, the American Medical Association and the Mi nesota State Medical Association.

Annual Meeting

SOUTHERN MINNESOTA MEDICAL ASSOCIATION

September 23, 1972—Austin, Minnesota

8:15 A.M.	Registration
9:00 A.M.	Opening remarks and announcements
9:05 A.M.	Transcystic Choledochostomy Mansur Taufic (Austin)
9:20 A.M.	Unusual Causes of Pain in the Wrist Ronald L. Linscheid (Rochester)
9:40 A.M.	Management of Urethral and Genital Injuries, David C. Utz (Rochester)
10:00 A.M.	Urinary Tract Infections and Reflux; A Pediatrician's Viewpoint E. C. Burke (Rochester)
10:20 A.M.	The Review of Mortality and Results in Aortic Coronary Shunts in 41 Patients over 65 W. Robert Schmidt (Minneapolis)
10:40 A.M.	INTERMISSION—Coffee and rolls
11:00 A.M.	Panel: Elective Sterilization Laparoscopy and Tubal Resection Carl E. Johnson (Rochester) Vasectomy and Its Criteria Laurence F. Greene (Rochester)
12:15 P.M.	LUNCHEON
1:30 P.M.	BUSINESS MEETING
2:00 P.M.	Villous Tumors of the Rectum—Technique and Results of Surgical Therapy Stan Goldberg, Jerry Schottler and E. G. Balcos (Minneapolis)
2:20 P.M.	C.E.A. Antigen for Detection of Cancer Allan J. Schutt (Rochester)
2:40 P.M.	Subcutaneous Mastectomy and Reconstruction with Silicone Prosthesis James K. Masson (Rochester)
3:00 P.M.	Finger-tip Problems David P. Anderson (Austin)
3:20 P.M.	INTERMISSION—Coffee and rolls
3:40 P.M.	Hypercalcemic Syndromes—Evaluation and Management Donald A. Scholz (Rochester)
4:00 P.M.	Panel: Interaction of Obstetrician and Pediatrician in High Risk Pregnancy The Care of the High Risk Pregnancy L. A. Aaro and R. S. Sheldon (Rochester) Intensive Care of the Distressed Infant Robert H. Feldt (Rochester)

Neurological Grand Rounds

Temporal Lobe Seizures

RUSSELL B. BUTLER, M.D.

"And one of the multitude answered and said, 'Master, have brought unto thee my son, which hath a dumb irit. And wheresoever he taketh him, he teareth him; d he foameth and gnasheth with his teeth, and pineth ay. And I spake to thy disciples that they should cast n out; and they could not . . .'

"And they brought him unto Him; and when he saw m, straightway the spirit tare him, and he fell on the ound and wallowed foaming.

"And He asked his father, 'How long is it ago since is came unto him?' And, he said, 'Of a child. And oft nes it hath cast him into the fire, and into the waters, destroy him; but, if thou canst do anything, have mpassion on us and help us.'" Mark 9:17.

S IS EVIDENT from this quotation, man is known have had seizures since ancient times but, even ough the malady has been known for centuries, remains a source of awe and mystery even day. Hippocrates was among the first to recog- ze that epilepsy was somehow related to the rain. In the 19th century, Hughlings Jackson was ble to correlate certain areas of the brain with ecific epileptic manifestations. The mapping brain areas by sequence of symptoms during izures was done by Jackson and carries the onym "Jacksonian march."

In recent years, a reaction against Jackson's ethod of localizing seizures has arisen. Physicians ay see only the final expression of a seizure and ey should not infer that the area of abnormality necessarily localized to that part of the brain om which the clinical signs seem to be mani- sted. The seizure activity, seen clinically, may ll relatively little about where abnormal dis- harges arose. Yet, there is a type of seizure, the linical expression of which may indicate involve- ent of the temporal lobe.

Balaam was said to have "seen the vision, and ell into a trance, but with his eyes open" (Num- ers 24:4).[6] This may have been the first descrip- ion of temporal lobe epilepsy.

The symptom complex which eventually was ttributed to the temporal lobes was more ade- quately described in the 1870's by Saunders in Germany, and soon thereafter by Hamilton in he United States, and Anderson in England. Hughlings Jackson first correlated these symptoms with pathology in the temporal lobes of man. The symptoms that Jackson described in one case included olfactory and visual hallucinations, automatic movements, a dreamy state which had the feeling of "old scenes reverting" and the sensation of a "panorama of something familiar and yet strange," vertigo and gastric sensations, and temporary insanity. The patient was demonstrated to have a tumor at the extreme anterior end of the right temporosphenoidal ridge, involving the amygdaloid nucleus. Jackson later suggested the term "uncinate group of fits" to include these symptoms.[6]

The human temporal lobe has three phylogenically distinct areas, the rhinencephalon, the limbic system and the neocortex. Yakovlev referred to the same three areas respectively as the entopallium, the mesopallium, and the ectopallium.[25,27] These areas are not confined to the strict anatomical limits of the temporal lobe.

The most ancient phylogenetic area is the rhinencephalon or entopallium. This includes the olfactory-visceral forebrain and the amygdala. Functionally it is related to olfaction. In man this area is connected to the anterior hypothalamus and thereby with the parasympathetic system. It is also interconnected with the sympathetic nervous system by way of the posterior hypothalamus. The reticular activating system which subserves consciousness may also be connected to the rhinencephalon by way of the posterior hypothalamus. The entopallium, by its spontaneous activity or by interconnections, has an effect of cellular metabolism, circulation, movement of viscera, incretion, excretion and secretion. The tissue structure of this system is primitive, consisting of unmyelinated fibers with numerous interconnections and synapses.[25] Experimental stimulation of this system has produced masticatory movements, olfactory hallucinations and the loss of consciousness.[26]

The next area of the temporal cortex to develop phylogenically was Broca's limbic lobe, a part of the limbic system of Papez. This is the mesopallium described by Yakovlev and composed of the hippocampus which is believed to be important

From Neurological Service, Veterans Hospital, Minneapolis.

in memory and learning. There are interconnections through the hippocampal gyrus, the alveus and the fornix to the mammillary bodies, the anterior thalamus and cingulate gyrus. These areas appear to subserve sympathetic responses and conciousness. There are also interconnections with the orbital frontal areas and with the basal ganglia. The tissue is composed of more complex, longer fibers which are myelinated.[25] There have been several attempts to determine function by stimulation experiments, but no consistent results have been noted. Bilateral removal of this system, however, results in marked impairment of recent memory. Functionally, this is the area that may be construed as serving the outward expression of the internal state best exemplified by the "fight or flight" reflex, thirst, pain, fear, pleasure and other modalities of emotionality.[26]

The neocortical area of the temporal lobes (ectopallium of Yakovlev) is composed of the superior, middle, inferior and fusiform gyri.[27] These are directly connected to the frontal lobe by the uncinate fasciculus and to the occipital lobe via the inferior longitudinal fasciculus. Within this area of the dominant hemisphere is the transverse gyrus of Heschel which serves in the perception of auditory inputs. The cellular components of ectopallium are well myelinated and run in parallels through the nervous system.[25] Stimulation of this part of the temporal lobes may cause a variety of results. If Heschel's gyrus is stimulated, non-differentiated sounds or vertigo result. Occasionally stimulation more anterior to the gyrus of Heschel will cause more complex auditory hallucinations of voices, sounds or even music.[6,26] Visual hallucinations occur with stimulation of the posterior half of the temporal lobe. Occasionally visual illusions of micropsia or macropsia also occur. Fear and pleasure have resulted from stimulation of the anterior temporal pole.[26] Yakovlev considers this area to be the "sphere of effectation" which is able to affect the outside world by means of expression and work.[27]

The temporal lobes are connected widely to the sensory inputs of smell, hearing, vision, the viscera and the autonomic nervous system. Neurons carrying sensations converge within the posterior areas of the temporal lobe, become intermingled and then pass anteriorly. The anterior areas may serve an "executive" or "elaboration" function. Stimulation of the neocortex in the anterior parts of the temporal lobe will cause vivid and elaborate hallucinations of auditory, visual and visceral sensations.[21,25,26]

Clinical Manifestations

Hallucinations

These may be olfactory, gustatory, visceral, cephalic, visual, auditory or vestibular. The olfactory hallucinations are generally described as being unpleasant, and this hallucination as an isolated event is rare. Gustatory sensations are described as metallic, acid or bitter. Visceral hallucinations include nausea, abdominal distress, hunger, tachycardia, or the sensation of a full bladder. Cephalic hallucinations such as swelling, pressure or heat in the head may arise. Pure visual and auditory sensations may also occur.

Illusions

These are false precepts of existing stimuli and may be of visceral spatial-temporal nature or even of a visual nature. The spatial-temporal illusions may be manifested by the sensation of "deja vu" (the sensation of familiarity in a strange place) or "jamais vu" (the sensation of strangeness in a place that should be familiar). Macropsia or micropsia (as well as vertigo) may also occur.

Aphasia of Various Types

Aphasia after a seizure may be caused by exhaustion of the neurons after the prolonged stimulus of the seizure. Dysphasia, characterized by a speech automatism, with sterotype and repetition of words or by phrases of irrelevant content or context, may also occur.

Emotional Experiences

The emotional undertones of the temporal lobe seizure are characteristic of the disorder. Usually it is a further manifestation of the sensory hallucinations and illusions. The olfactory sensation may appear to be foul and even nauseating; the visceral sensations become strange and are, perhaps, associated with fear, rage or pleasure. Sexual experiences have been described.

Amnesia

Amnesia is one of the hallmarks of the temporal lobe seizure. There are two possible explanations. The anatomical localization of the hippocampus and the hippocampal gyrus in the temporal lobe may make these areas vulnerable to abnormal discharges and cause disruption of their memory function. Williams[25] advocated another concept: most of the symptoms of the psychomotor seizure are usually related to the personalization of the experience, or the "I am."

f this functioning is disrupted during the seizure, hen the inverse, or the "I am not" can be the symptom manifested. This would be expressed as amnesia for the event.

Automatisms

These are motor movements in association with the temporal lobe seizures. Possible interconnections with the motor cortex by way of synapses through the basal ganglia and the prefrontal cortex may account for the movements, which can be simple repetition such as smacking the lips or more complex ones which are repetitive and purposeless.

Disordered Behavior

The most complex and most debated symptom of the psychomotor seizure is that of disordered behavior. This is allegedly a manifestation of the automatisms, with an overplay of the emotions of rage or pleasure-seeking. Kluver and Bucy demonstrated that bilateral anterior temporal lobectomy in monkeys caused memory loss and passiveness. The correlation of psychopathic personality, mainly with temporal lobe foci, has been described in convicts with abnormal electroencephalograms.[8] Severe personality problems and antisocial behavior are felt to be more prevalent in patients with temporal lobe seizures.[23] There has also been considerable acceptance that types of "hyperkinetic impulsive behavior" may often be associated with abnormal electroencephalograms having temporal lobe foci.[16]

Sexual deviation has been described in association with damage to the temporal lobes.[11] In many of the instances of distorted personality and behavior the problem arises of determining if the entire personality is changed by the interictal disease as well as by the ictal state. There is reason to believe that some of the manifestations of the temporal lobe seizure may be continuous, and clinical only in that it is causing the patient to incorrectly perceive his environment. Hill[14] has suggested that the abnormal personality, the psychopathic aggression and antisocial behavior may be better correlated with abnormalities in the posterior part of the dominant temporal lobe. It is fallacious, however, to state that every person with temporal lobe seizures has a distortion of personality. Many well-adjusted and productive people are known to have the disease and live within the society.

Treatment

The treatment of the psychomotor seizure is difficult.[6] Celsus described epileptics of Rome drinking blood from fallen gladiators as a form of treatment. However, modern physicians use better medical measures; or surgery may be considered when medicines fail. About 11% of patients with temporal lobe seizures will have a poor response to medical therapy. Another 50% will have only a fair response to the medications now available.[15] Currently favored treatment of psychomotor seizures include: Dilantin (R), (diphenylhydantoin) Mysoline (R) (primidone) and Tegretol (R), (Carbamazepine). (The use of Tegretol for this disorder has not been approved by the Federal Drug Administration.) Often phenobarbital is added to the regimen. Mesantoin (R) (mephenytoin) and Phenurone (R) (phenaceamide) have also been used with varying success but are more toxic.

Anticonvulsants

The mechanisms whereby anticonvulsants work are slowly being elucidated.[14] Hydantoins may enhance extrusion of sodium from the cell, thereby hyper-polarizing the cell membrane; they may also reduce the ability of cells to respond to repeated tetanic stimuli, thereby preventing the spread of impulses.[15] The barbiturates and Mysoline (R) seem to be effective in preventing the depolarizing effect of acetylcholine at the synaptic junctions; perhaps they also stabilize the membrane by slowing the transport of sodium and potassium. The effect of repetitive discharges may be reduced.[15]

Anterior Temporal Lobectomy

Generally the anterior temporal lobe is removed back to the vein of Labbe, or about 5.5 to 8 cm from the temporal horn. The degree of success ranges from 43% to 53% in different series. The procedure is unilateral, as bilateral lobectomy causes severe memory loss and other undesirable effects. Some psychiatric disorders associated with the seizure disorder may improve. In about 45% of the patients with pre-existing psychiatric problems, improvement of their interpersonal relations followed. Others, including Meier,[18] have presented data based on the Minnesota Multiphasic Personality Inventory profiles and Psychopathological indices to suggest some decline in the schizo-adaptive behavior characteristics.

The complications of the surgical procedures have been visual field losses; occasionally, left-sided operations will result in dysphasia or even deficits in learning by auditory stimuli.

There was improvement in the electroencephalogram (EEG) in many of the cases, and the EEG has become one of the tools by which prognosis after the operation can be formulated. The surgical procedure usually includes the removel of the deeper structures, the uncus, amygdala and anterior hippocampus. The patients with removal of this area also seem to do better over the long run; those who had a rightsided EEG focus and subsequent removal of the right anterior temporal lobe do better than those with leftsided lesions[4] Mullan [20] has recommended ablation of the lateral nuclear mass of the thalamus and the ventral anterior subthalamic areas.

Temporal lobe seizures are most commonly seen in young adults; however, in 37% of one series,[2] symptoms could be traced back to before the age of 11 years. Another 35% of the patients had abnormalities such as social and verbal underdevelopment, enuresis or sleepwalking. A high incidence of birth trauma (51.3%) was reported in patients with psychomotor seizures.

Pathology

Sclerosis

As early as 1825, Bouchet and Cazauvieihl described sclerosis in the hippocampus of an epileptic patient. In 1880 Sommer gave his name to the area of pyramidal cells of hippocampus which had been noted to have degenerated in patients with "idiopathic" seizures. Since that time there have been several series composed of autopsy and post-surgical specimens from seizure patients with what is now called "Ammon's horn sclerosis." The cause, according to Earle, Baldwin and Penfield,[7] is herniation of the hippocampus into the tentorial opening during molding of the head at birth, which produces either direct pressure or arterial compression with anoxia and which may cause scaring to the temporal lobe tip. Other workers have reported that closed intracranial injuries, encephalitis, or chronic sinusitis[26] may produce damage to the same area.

Atrophy

About 40 to 50 percent of patients with temporal lobe seizures have atrophy of the inferior and medial aspects of the temporal lobe. According to Meyer [19] the lesions in the temporal lobe may show subpial or marginal gliosis in which glial tissue is increased in the first cortical layer, along with nerve cell loss, and subcortical gliosis, in which there is a proliferation of astrocytes and the loss of axones in the white matter.

Neoplasms

About 12 to 18 percent of cases show neoplasms in association with the seizure disorder. The patients with classical uncinate fits have a higher incidence of low-grade gliomas. About 5% or less are associated with vascular malformations. About 20% have no demonstrable lesion.

Electroencephalogram (EEG)

Gibbs, Gibbs and Fuster[13] were among the first to correlate the EEG with temporal lobe seizures. About 95% of the patients studied at the Montreal Neurological Institute had an abnormal EEG which correlated well with their clinical symptoms. Of these, 80% had foci in the anterior-inferior-medial temporal areas and 15% had discharges seen in the posterior or middle temporal areas. Hill[14] described an EEG pattern which is present in 46% of the patients with temporal seizures: an initial generalized voltage suppression followed by generalized rhythmical slow-waves which progressively increase in amplitude and decline in frequency, followed by abrupt onset of generalized flattening for several minutes. The record then returns to a normal inter-ictal pattern. Gastaut[12] states that as many as 25% of patients will show no characteristic changes on EEG. Woolsey[26] noted that active seizure discharges deep in the anterior medial temporal lobe may have no electrical counterpart on the cortical or scalp electrodes. This may account for Gastaut's observation.

Comments

The current problems with drug abuse has added interest and concern to the problems of the temporal lobe seizures. There have been postulations that compounds such as Lysergic Acid Diethylamide (LSD-25), Psilocybin and Psilocin may be causing a form of temporal lobe seizures.[1] Demonstrations with cats have shown that LSD-25 administration results in seizure activity recorded with implanted electrodes in the amygdala, entorhinal cortex and parts of the hippocampus. There is further evidence that these three compounds have their effect by means of the temporal lobes since the temporal lobes have to be intact to produce clinical symptoms, as it has been demonstrated that LSD-25 will not have an affect in chimpanzees who have had bitemporal lobectomies.[3]

See references on page 762.

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Book Reviews

UNDERSTANDING LABORATORY MEDICINE, Camillo V. Bologna, M.D. C. V. Mosby Co., St. Louis, 1971, 259 pages. $9.80.

Written by the Director of Laboratories of St. Ansgar Hospital of Moorhead, and St. Francis Hospital of Breckenridge, Minnesota, this book is geared primarily for paramedical individuals and for physicians desirous of some conceptual understanding of laboratory medicine. Though the volume is geared for the professional, the level of approach is often too elementary. While the title purports to convey an understanding of the broad field of laboratory medicine, the contents touch only very superficially on the areas of blood banking, genetics, microbiology, and serology-immunology. It is possible that the author has responded less to these areas of laboratory medicine because the questions and discussions which he relates provided the stimulus for this volume were not forthcoming in these disciplines.

The author's conceptual approach to his topic is an interesting one. The chapters proceed from the normal cell and its milieu to "the cell community as a body," at the same time embracing some physiology, biochemistry, pathology and philosophy. Electrolyte, acid-base and fluid balance are then discussed. Subsequently he deals with bone, muscle and very briefly protein. At this point one has covered one-third of the volume. Chapters then deal with the circulatory system, hematology, liver disease, a lengthy chapter on hormones, and a brief discussion of enzymes of clinical importance. The role of man in the biosphere is interposed between the cellular fluid milieu and the discussion of mesodermal structures.

Although the author states that he does not wish to go into methodology, some discussion of the specimens used, and specimen collection, subjects much misunderstood in laboratory medicine, would have been very useful to the individuals for whom this book was written.

The reviewers would also challenge certain points made by the author. Among these, and for example, we believe that urinary urobilinogen is *increased* in hemolytic disease and *decreased* in extrahepatic obstruction. We also doubt that 2% acetic acid will dissolve yeast as well as red blood cells.

G. Mary Bradley, M.D.
John M. Matsen, M.D.
Minneapolis, Minnesota

INTRODUCTION TO HEMATOLOGY by William M. Dougherty, C. V. Mosby. $10.50.

The author states that this is an introductory book designed for the beginning student and written to promote understanding without necessity for rote memorization. Although he has covered a large volume of material with a concise text, I do not think that it promotes an easy understanding of the subject of hematology. He eliminates the discussion of a number of items which should be present in an introductory hematologic text and which the beginning student could not be expected to know without some prior exposure to hematology and hematologic laboratory techniques.

The illustrations are black and white photographs, many of which have poor definition. In introducing a person to the identification of blood cells, a small number of good colored photographs is superior to an over-abundance of black and white photographs. The legends explaining the illustrations are cumbersome, often placed on pages removed from the figure which they are describing and are too lengthy.

I recommend this book review for the physician or paramedical person who has a background in hematology but who wishes to bring himself up to date with current changes. However the author includes little comparison of current terminology with prior definitions changed within recent years.

John H. Brown, M.D.
St. Louis Park, Minnesota

FORUM. The International Journal of Human Relations. Vol I, No. 4 January 1972. London.

Forum Volume 1 Number 4 is the January, 1972 issue of a new journal of uncertain age. Volume I suggests a new journal, but the inside front cover consists of an advertisement for back numbers at $1.00 each for issues of Volumes 2, 3, and 4. Forum seems to be London's answer to the U.S.A.'s publication "Medical Aspects of Human Sexuality," a collector's item which has appeared unsolicited on my desk since 1967. One title of the table of contents should suffice to establish the titillating quality and character of Forum: Learning to last—ejaculation control techniques. If Forum were illustrated it would rate a Hollywood X. A proper review would lead the printer to mail MINNESOTA MEDICINE in a plain wrapper.

Reuben Berman, M.D.
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DRUGS OF CHOICE by Walter Mondell. C. V. Mosby Co., St. Louis, publisher, $17.75, about 900 pages.

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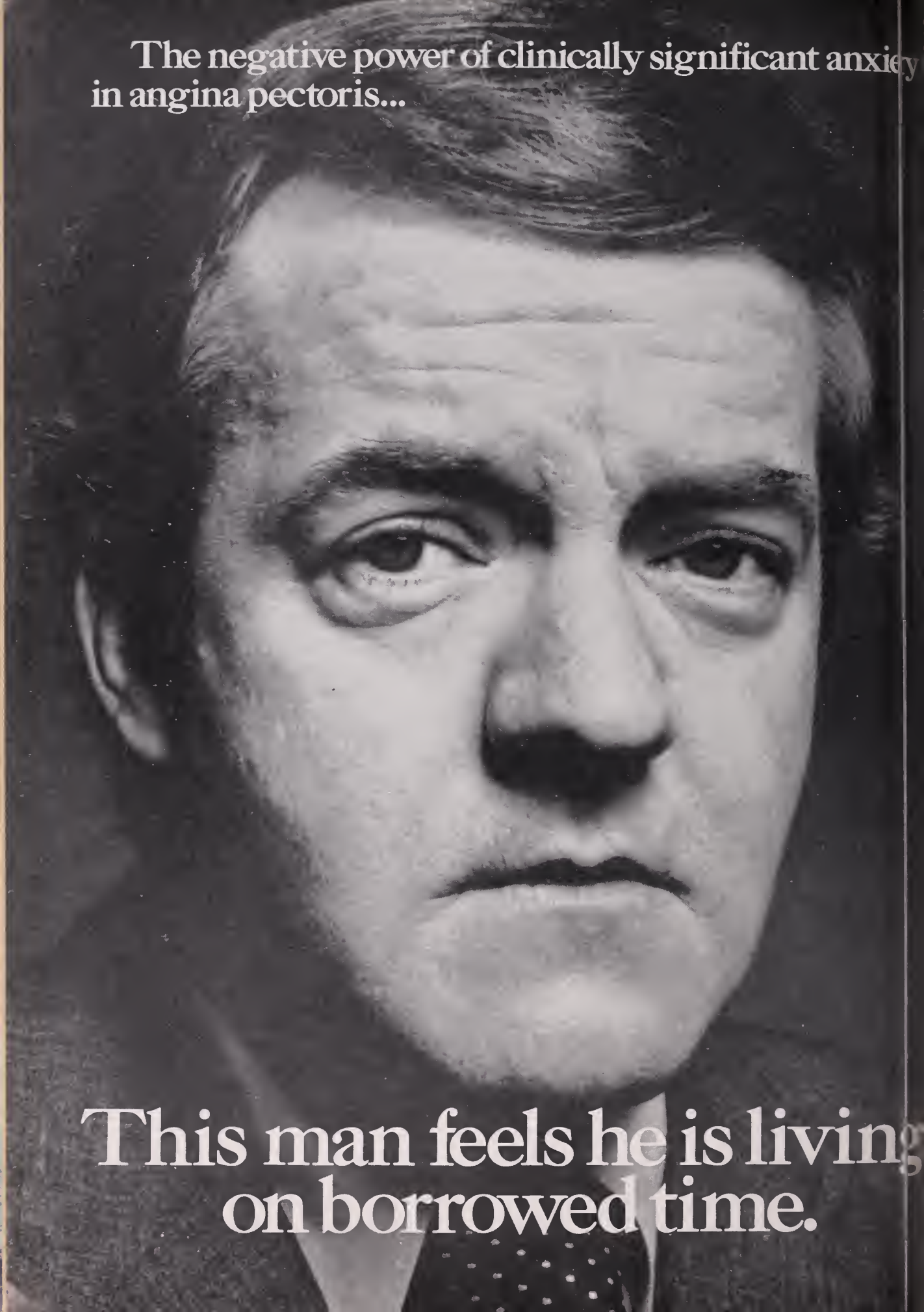
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Harry B. Clark, M.D.

SEPTEMBER, 1972


The negative power of clinically significant anxiety in angina pectoris...
This man feels he is living on borrowed time.

During anginal attacks, patients may suffer intense apprehension. More frequently, however, they experience a continuing sense of less severe but nonetheless disproportionate anxiety.

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Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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*Levine, S.: "Angina Pectoris and Emotional Overlay," Scientific Exhibit presented at the Annual Meeting of the Maine Medical Association, Kennebunkport, Me., June 13-15, 1971.

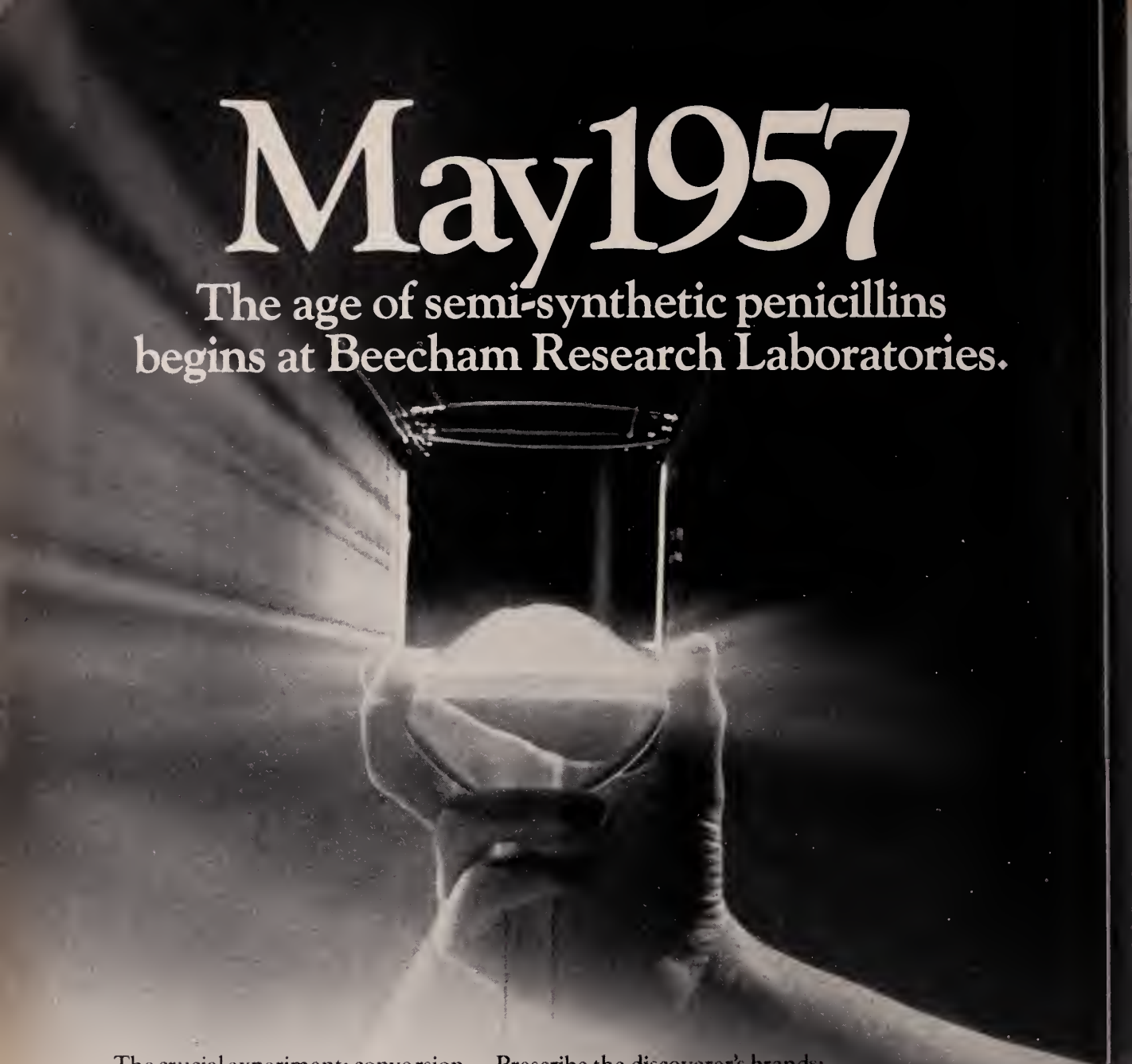
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Precautions: 1. *Starvation Ketosis:* This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of relatively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**

2. *Lactic Acidosis:* This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.

3. *Hypoglycemia:* Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.

Adverse Reactions: Principally gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake.

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of moderate to severe intensity

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a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few of patients in association with the use of Talwin although no causal effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®) may be of value if respiratory depression occurs.

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President's Letter



Minnesota Physiatric Society

The Minnesota Physiatric Society is pleased to be included in the list of organizations now represented by Minnesota Medicine. The term "physiatric" may be new to some. It refers to the Physiatrist, a physician who practices the specialty of Physical Medicine and Rehabilitation. Although the Minnesota Physiatric Society is quite young (founded in 1964) the specialty itself is not so new. The American Board of Physical Medicine and Rehabilitation was established under the Advisory Board of Medical Specialties in 1947 and the first Board examinations were conducted in Minneapolis that year.

Before the late 1950s many thought of this specialty as being mainly involved with poliomyelitis. Since that disease has been virtually eliminated, Physiatry has become better known for its work with such patient problems as spinal cord injury, strokes, amputations, joint disorders, and many of the degenerative disorders of the neuro-musculo-skeletal systems. Physical Medicine and Rehabilitation as a specialty has been involved in the application of physical sciences to medicine; for example, microwave (radar), ultrasound, and the use of electronics in the diagnosis of nerve and muscle disorders known as electromyography and electroneuronography. It has widely broadened the understanding and therapeutic application of the physiology of muscle and physiology of exercise.

Minnesota physiatrists have played a prominent role in the development of Physical Medicine and Rehabilitation as a medical specialty. Dr. Frederic J. Kottke, Professor and Head of the Department of Physical Medicine and Rehabilitation at the University of Minnesota, served on the American Board of Physical Medicine and Rehabilitation from 1955 to 1969. Dr. Frank H. Krusen, Founder of the Section on Physical Medicine and Rehabilitation of the Mayo Clinic, played a leading role in establishing the present Section of Physical Medicine and Rehabilitation in the American Medical Association. Dr. Glenn Gullickson, Director of the Rehabilitation Center, University of Minnesota Hospitals, served as the Executive Director of the American Congress of Physical Medicine and Rehabilitation from 1960 to 1965. Dr. Paul Nelson, Cleveland, Ohio, Editor of the Archives of Physical Medicine and Rehabilitation, has served as the Editor of the Archives since 1953. He is a native of Minnesota, having received his medical schooling and specialty training at the University of Minnesota and the Mayo Foundation. The Handbook of Physical Medicine and Rehabilitation is authored by three prominent Minnesota physiatrists; Drs. Krusen, Kottke and Ellwood. Dr. Miland Knapp, the pioneer in this field for Minnesota as well as a leader in national organizations, has for the past decade participated in an unusual program of continuing education for physicians in rural and small communities.

For many years the state of Minnesota has had the highest proportion of board certified physiatrists per capita of any state in the U.S.A. The Minnesota Physiatric Society now has 48 members. Most of these physiatrists are concentrated in the Twin Cities and Rochester.

Thomas P. Anderson, M.D.
President
Minnesota Physiatric Society

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—George Sarton, from "The History of Medicine Versus the History of Art"

Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

13.3%
Yes, it would be useful.

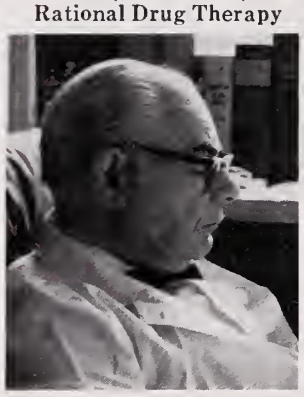
86.7%
No, it would not be useful.

Dialogue

Would it be useful in clinical practice to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy in practice can rea determined.

The Bureau of Dr suggested the packa sert as a possible m communicating infor on relative efficacy o to the physician. I fi objectionable, since not believe the ph should have to rely source for final sc truth. There is also tical objection: Sin physicians actuall pense drugs, they see the package ins any event, I would tain that the phy should know what d wants and why witho pending on the gover or the manufacturer him.

Undoubtedly, phys are swamped by exc numbers of drugs in therapeutic categorie I am well aware that drugs within such at gories could be elim without any loss, o haps even some pr the practice of me But, in my opinion, n the FDA nor any th single group has the tise and the wisdom sary to determine th "drug of choice" i areas of medical prac

Maker of Medicine

n th G. Kohlstaedt, M.D.,
Vice President,
edical Research,
E Lilly and Company



I my opinion, it is not e nction of any governor private regulatory e y to designate a "drug c ice." This determinaon hould be made by the ysician after he has re- l full information on e roperties of a drug, n hen it will be based on s xperience with this r and his knowledge of e ndividual patient who s king treatment.

I n evaluation of com- a ive efficacy were to be a , particularly by gov- n ent, at the time a new r is being approved for a eting, it would be a r disservice to medi- n nd thus to the patient t consumer. For exam- e when a new therapeu- c ent is introduced, on e asis of limited knowl- g it may be considered e more potent, more f tive, or safer than r ucts already on the a et. Conceivably, at i time the new drug u l be labeled "the drug f oice." But as addi- o l clinical experience is c nulated, new evidence a become available. a r, it may be apparent that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audiovisual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use – information that the pharmaceutical manufacturers must begin to provide if government regulation of *"drugs of choice"* is to be avoided.

Opinion & Dialogue

What is your opinion, doctor?
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Cancer of the Colon and Rectum

Epidemiology and Possible Causative Factors

DENIS P. BURKITT

IN THE WESTERN WORLD CANCER is the second most common cause of death after cardiovascular disease.

With the exception of bronchial carcinoma, tumours of the large bowel are responsible for more deaths from cancer than any other form of neoplasm.

In the U.S.A. alone over 75,000 new cases of cancer of the colon and rectum are diagnosed every year.

A New Approach

In an effort to understand the mechanisms involved in malignant transformation of tissue cells, the emphasis in cancer research has tended to be at subcellular level. Admittedly, epidemiological studies have been attracting increasing interest, but those on men still receive less attention than those on mice. Even when epidemiological studies are given due prominence, specialization tends to blinker the cancer research worker that non-malignant disease is well outside his sphere of interest.[1]

Those responsible for cancer registries pay little attention to benign tumours and even less to other non-neoplastic disease. The electron microscope and other modern and sophisticated techniques enable the visualization of the minute and this approach has not been matched by an overall view of the problems confronting us. Our knowledge of twigs and leaves increases at the expense of understanding trees, let alone woods, or forests.

A malignant tumour, be it in breast, bladder or bowel, must be viewed in its relationship not only to benign companions but also to other diseases of the organ concerned and event to associated diseases affecting other parts of the body.

The Relevance of Relationships

Clues to the causation of a disease may be found by comparing its geographical distribution with that of a disease whose cause is already understood. This approach has tended to be overlooked, particularly in the field of cancer.

If two or more effects are produced by a common cause they will both or all be found to be associated with one another, where the common cause operates, but will be rare or absent where the cause is missing.

If two causes tend to be associated with one another all the effects of each will also tend to be associated.

Conversely, an observed tendency for certain diseases to be associated with one another epidemiologically suggests the possibility that they may be at least in part the result of common or related factors.

Moreover, if two or more diseases are the result of common or related factors they will both or all be found most frequently in the geographical regions or the sections of communities most exposed to the causative factors and will consequently be found together in individual patients more often than would otherwise be expected.

Conversely again, an observed association between certain diseases in individual patients suggests the possibility of a common or related causative factor.

Such observations can provide the foundations on which hypotheses of possible aetiology can be built.[2,3]

An attempt will be made to construct a hypothesis for the cause of large bowel cancer based on its relationship with some other diseases characteristic of modern western civilization. These include not only other non-infective disease of the colon and rectum such as benign tumours, diverticular disease, appendicitis and ulcerative colitis, but also such apparently diverse conditions as varicose veins, deep vein thrombosis, coronary heart disease, gallstones and obesity.

Presented at the United Hospitals and American Cancer Society, Ramsey County Unit, Cancer Symposium, St. Paul, March 28, 1972.

Dr. Burkitt is a member of the External Staff of the Medical Research Council of Great Britain, and is a Fellow of the Royal College of Surgeons of England.

See editorial, page 815.

Vultures and Carcasses

The simplest way to locate a dead animal in the African bush is to look for tell-tale vultures flying overhead. The known association between them enables the more easily found birds to be used as a guide to the more concealed carcass.

This same approach could be used epidemiologically if those investigating different diseases (corresponding to carcasses and vultures) were less exclusively specialized.

Let us consider some diseases associated with bowel cancer, which may play the part of the vultures around the carcass we wish to investigate.

Non-infective Diseases of the Bowel

Cancer and Polyps

Benign and malignant tumours of the colon and rectum are closely associated in so many ways that Morson and Bussey[4] consider them merely different manifestations of the same cause. They are closely associated:

In Anatomical Distribution—The distribution of both benign and malignant tumours of the colon and rectum are closely similar.[5]

In Individual Patients—There is a close association between benign and malignant tumours in individual patients.

Bockus et al.[5] found that whereas polyps were found in only 12% of cancer free colons in patients over the age of 45 years, they were found in 21-25% of colons with cancer in the same age group.

Similarly, Rider et al.[6] showed that cancer of the colon and rectum was 16 times as common in patients with polyps than in patients without polyps.

In Age Distribution—The age distributions of both benign and malignant tumours are very similar.[5]

Experimentally—Both benign and malignant tumours can be induced by the same substances in experimental animals.[7,8]

In Geographical Distribution—No form of cancer is so closely associated with modern economic development as cancer of the colon and rectum. The variations in ratio of colon and rectal involvement are small compared with the varying in incidence of large bowel cancer as a whole.

Throughout sub-Saharal Africa cancer of the colon and rectum accounts for about 2% of all malignant tumours[9] and this figure is not greatly influenced by age since most forms of cancers a more prevalent in later life.

Where bowel cancer is rare simple tumours a almost unknown.[10,11] Where the incidence of m lignant tumours increases that of benign tumou increases at a much greater rate, and consequent are present in over 10% of the adult population i countries with the highest rates of bowel cancer.

Cancer and Diverticular Disease

Cancer and diverticular diseases of the colo are closely associated:

In Anatomical Distribution—In regions whe they are both common their maximum frequenc is in the distal colon with diminishing frequenc towards the proximal colon.

In Sex Distribution—Both conditions are con moner in women.

In Individual Patients—Little has been done t relate cancer and diverticular diseases in individu patients. Parks and Connell[12] found 11 cases c cancer of the colon in 445 patients with advance diverticular disease, which is many more tha would be expected even in patients over the ag of 60.

Chronological Emergence—Diverticular diseas was rare in Britain and the U.S.A. until after th first world war. Since that time the frequency ha increased enormously.[13] It is not known whe bowel cancer first emerged as an important clinica entity in the western world. We do know how ever that some 30 years ago the frequency of bot cancer[14,15] and diverticular disease[16] in Americar negroes was only about half of that in the whit population, whereas today their incidence is com parable in the two races. This suggests that bot diseases may have increased during approximately the same period. Experience in developing coun tries suggests that cancer frequency rises a littl before that of diverticular disease.

Geographical Distribution—There is a very close association between the geographical distri bution of bowel cancer and diverticular disease Both have their maximum and minimum fre quency in the same communities and availabl information suggests that the same applies in area of intermediate frequency.

Appendicitis

Cancer of the colon and rectum and appendici tis are associated.

In Geographical Distribution—Both cancer o the large bowel and appendicitis have their maxi mum and minimum incidence in the same com-

unities.[9,17]

In Chronological Emergence—The frequency of appendicitis always rises many years before that of bowel cancer—never the reverse.

Even if both diseases were, as I believe, related to a common cause, this relationship in individuals would not be expected since they affect people at entirely different periods of life. Responsible environmental factors may be present in youth, but not persist.

McVay[18] (1970) did in fact detect an association between cancer of the bowel and previous appendicectomy. Those who suspect the diagnosis of chronic appendicitis would consider any such association of doubtful validity.

Ulcerative Colitis

This disease is very closely associated with cancer of the large bowel:

In Individuals—Over 40% of patients with extensive ulcerative colitis for over 25 years are said to develop cancer of the colon or rectum.[19]

In Geographical Distribution—Ulcerative colitis is almost unknown in areas where bowel cancer is rare.[20,21,22]

Possible Guides

Applying the principle of the vultures and carcasses referred to above, a search for the causes of diverticular disease and appendicitis may throw light on causes of tumours and ulcerative colitis.

In a search for the cause of bowel disease food is the first environmental factor to be considered, since this determines the nature of the faeces which contribute most to the environment of bowel mucosa.

Diverticular disease and appendicitis are rare or unknown in communities consuming high residue diets and have their highest frequency among those who have relatively recently changed from a high to a low residue diet.

Appendicitis rose in frequency in the western world shortly after the introduction of roller mills in the 1880s. This higher extraction process in making white flour removed nearly all the cereal fibre and in subsequent years the amount of bread consumed fell by about half. The frequency of appendicitis does not appear to rise in developing countries until white flour partially replaces traditional unprocessed carbohydrate foods.

Diverticular disease, in contrast to appendicitis, is a complaint of later life, and so presumably requires much longer exposure to the causative environment. In the U.S.A. it was little more than a surgical curiosity before the first world war and only became a well recognized clinical entity in the 1920s.[13] In developing countries it is almost confined to the top socio-economic groups who have to a large extent adopted western type food.

Since unabsorbable fibre is the fraction of food that reaches the colon with least change it is more likely to affect that part of the intestine than digestible components of food, little of which reach the large bowel. This fact, together with the observed relationship between removal of dietary fibre and a subsequent rise in frequency of diverticular disease and appendicitis, suggests that a fibre-depleted diet may be causally related to these diseases.

Food Fibre and Bowel Behaviour

Extensive studies in many countries in Africa and India and in different communities in England have demonstrated a direct relationship between dietary fibre and both intestinal transit time and stool weight and consistency.[9,23,24,25,26] African villagers on a high-residue, little-processed diet have been shown to pass 80% of swallowed radio opaque markers within about 30-40 hours and to evacuate on average 300-400 gms of unformed stool daily.

Volunteers on standard English diet had intestinal transit times averaging over 70 hours and evacuated less than 150 gms of formed stool daily.

White students in South Africa, Indian nurses in India, vegetarians in England and more educated Africans on a mixed diet, showed intermediate figures in both intestinal transit times and stool weights.[26]

Postulated Mechanisms Relating Non-infectious Diseases of the Bowel with Dietary Fibre

Diverticular Disease

Painter[27,28,29] has shown the manner in which the colon contracts in response to small firm faeces. These contractions form closed segments in which high pressures are built up and it is these that are believed to cause protrusions of mucosa through the muscular wall.

Appendicitis

A similar mechanism is believed to be responsible for appendicitis.[17,30] Intraluminal pressures can build up behind an impacted faecalith (a product of low residue diet), a stricture or pre-

sumably muscular contraction similar to that demonstrated in the colon. Mucosa devitalised by these pressures would be vulnerable to bacterial invasion. It has been postulated that alterations in bacterial flora of the faeces due to dietary changes may be a contributory factor.[31]

Benign and Malignant Tumours

As pointed out above there are strong grounds for suspecting common aetiological factors for benign and malignant tumours.

Any acceptable hypothesis must take into consideration the following facts:

(a) the rarity of these tumours in developing countries and in animals;

(b) the relationships between tumours and other non-infective diseases of the large bowel;

(c) the relationship between the incidence of intestinal cancer and the fibre content of diet;

(d) the rarity of cancer in the small intestine;

(e) the much greater differences between increase in frequency of tumours in the distal colon relative to the proximal colon when comparing areas of high and low overall incidence;

(f) the much smaller difference in colon/rectum ratios in different communities than in overall incidence of large bowel tumours;

(g) the observation that in rats maintained in a sterile environment no tumours develop, following administration of substances that produce tumours in the colon and rectum of normal animals.[32,33] This suggests that bacteria play an important role:

(h) the differences between the bacterial flora in stools from communities with high and low risks of developing bowel cancer;[34,35,36]

(i) the fact that some 30 years ago negroes in North America had a much lower frequency of large bowel cancer than the white population.[14,15]

The following suggested mechanism would be consistent with these observations:

The rarity of tumours in the small bowel and the almost total absence of epithelial tumours suggests that the factor responsible for inducing tumours is not ingested, since its action only becomes apparent in the colon and increases towards the distal colon.

A carcinogen dependent on bacterial activity would be largely limited to the colon and rectum, whereas ingested carcinogens would be expected to act on the small intestine.

A carcinogen formed in the large bowel would increase in intensity from the proximal to the distal portions, and might be expected to have its maximum effect in the sigmoid colon and rectum. When faecal arrest results from a low residue diet, any carcinogens in the faeces would be held in particularly prolonged contact with the mucosa of the sigmoid colon in a concentrated form in a small faecal mass. It is here that maximum tumour incidence is found.

It has been shown that the bacteria which are more numerous in the stools from areas with a high frequency of bowel cancer can degrade bile salts to substances known to be carcinogenic. Any faecal arrest would not only provide more time for proliferation of bacteria, but also for their action on bile salts. The bacterial changes may also reflect alterations in the nature of the bowel content due to the quality of food eaten.

Additional Incrimination of a Fibre-depleted Diet

Cancer and other non-infective diseases of the large bowel are epidemiologically associated with varicose veins, deep vein thrombosis, coronary heart disease, gallstones and obesity. Can fibre be considered as a causative factor in any of these diseases associated with bowel cancer but not involving the gastrointestinal tract?

As shown above, faecal arrest results in increased pressures within the bowel lumen, and also causes raised intra-abdominal pressures during straining at stool. Since raised intra-abdominal pressures are readily transmitted down the leg veins after the valves have become incompetent they must be taken by the valves when still competent. Such pressures could lead to valvular incompetence with resultant changes in the superficial veins recognized as varicosities and in the changes in the deep venous plexuses which in the presence of venous stagnation may predispose to thrombosis.[37] Here again, fibre deficiency could be an important causative factor.

High levels of serum cholesterol are also associated with low residue diets and vice versa. A relationship between cholesterol metabolism and dietary fibre[38] could explain the association between bowel cancer and both coronary heart disease and cholesterol gallstones.

Removal of fibre from carbohydrate foods almost inevitably results in overconsumption of the refined product. This may explain the association of diseases presumably caused by overconsumption of starch and sugar with those caused by a fibre-deficient diet.[31] Obesity diabetes and dental

aries are closely related to overconsumption of efined carbohydrate.

Conclusion

The argument outlined above, incriminating a ibre-deficient diet in the cause of bowel cancer, consistent with epidemiological and other evience.

This suggests that a return to a high residue diet nd particularly to wholemeal flour might not only ignificantly reduce the frequency of America's second commonest cause of death from cancer but also that of many other major health problems of this country. Moreover, if communities in developing countries could be persuaded not to copy indiscriminately the food habits of the more economically developed countries, in particular the consumption of refined carbohydrates, future generations might be saved from suffering in endemic proportions some diseases characteristic of modern western civilization.

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"You are old, Father William," the young man said,
"And your hair has become very white;
And yet you incessantly stand on your head—
Do you think, at your age, it is right?"
"In my youth," Father William replied to his son,
"I feared it might injure the brain;
But now that I'm perfectly sure I have none,
Why, I do it again and again."*

*From Lewis Carroll's: Your are old, Father William.

Left Ureteral Obstruction

Following Ileac Diversion

LLOYD C. GILMAN, M.D., GERALD W. IRELAND, M.D. AND
ALEXANDER S. CASS, M.D.

THE GREATER INCIDENCE of obstruction of the left ureter following ileac diversion has been documented[1] and attributed to angulation of the left ureter as it coursed through the sigmoid mesentery.

Five cases of left ureteral obstruction with secondary pyelonephritis or stone formation have occurred in 87 ileac diversions performed during the last five years at St. Paul Ramsey Hospital and Gillette State Hospital for Crippled Children. Exploration in three of these cases has revealed an obstruction of the left ureter as it passed under the inferior mesenteric artery.

Department of Urology, St. Paul Ramsey Hospital; and Urology Service Gillette State Hospital for Crippled Children, St. Paul and University of Minnesota Medical School, Minneapolis.



Fig. 1 (Case 1)—Excretory urogram showing delayed function in the left kidney and a possible left ureteral stone.

Case Reports

Case 1

A 35-year-old male with traumatic paraplegia and a neurogenic bladder of 16 years' duration had an ileac diversion performed in October 1967. In May 1969 radiological evaluation revealed a stone in the left renal pelvis and the patient refused surgery. In November 1969 he was admitted with left pyelonephritis and further radiological evaluation revealed an obstruction of the middle one-third of the left ureter with the stone immediately above this area (Figures 1 & 2). The stone was removed at surgical exploration through a ureterotomy in the upper ureter and an obstruction to the ureter was found where it passed under the inferior mesenteric artery. Division of the inferior mesenteric artery relieved the obstruction and postoperative excretory urograms showed no obstruction of the ureter.



Fig. 2 (Case 1)—Retrograde ileostogram demonstrating an obstruction in left ureter.

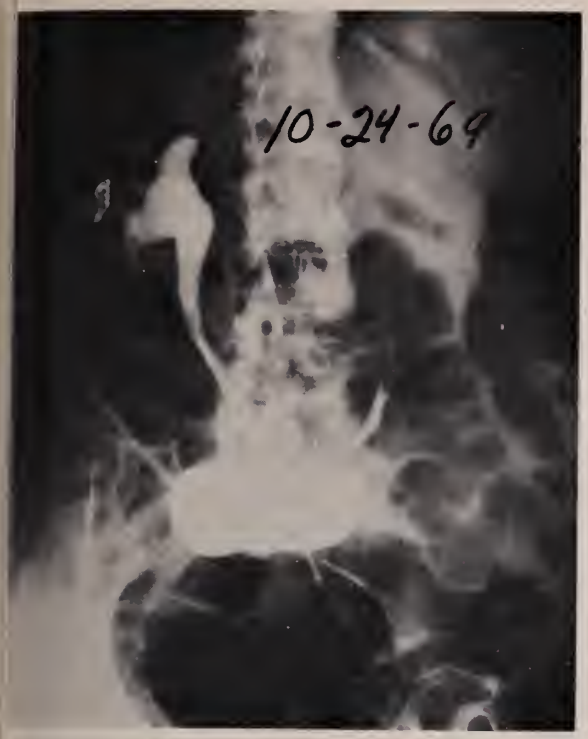


Fig. 3 (Case 2)—Retrograde ileostogram showing an obstruction in the left ureter.



Fig. 4 (Case 3)—Excretory urogram revealing dilated upper left ureter and calyces with a stone present in the ureter.

Case 2

A 45-year-old female with a neurogenic bladder due to multiple sclerosis had an ileac diversion on May 11, 1967. She was admitted with left pyelonephritis on October 1969. Excretory urogram and retrograde ileostogram (Figure 3) demonstrated an obstruction of the middle one-third of the left ureter with a stone in the proximal ureter. At exploration the stone was removed from the renal pelvis and an inflammatory stricture was found in the ureter where it passed under the inferior mesentric artery. The stricture was treated by a Davis intubated ureterostomy. Postoperative excretory urograms showed no dilatation of the left ureter.

Case 3

A 47-year-old female with multiple sclerosis and a secondary neurogenic bladder had an ileac diversion performed on January 16, 1969. She was admitted with left pyelonephritis on October 26, 1969 and radiological evaluation demonstrated a stone and left hydronephrosis above the obstruction of the middle one-third of the ureter (Figure 4). At exploration the stone was removed through a ureterotomy in the upper ureter and an obstructing inferior mesenteric artery was divided. No dilatation of the ureter was present on subsequent radiological examination.

The two remaining cases have each had one attack of pyelonephritis and radiological evaluation has revealed a relative obstruction in the mid third of the left ureter with only slight dilatation of the left ureter above this point. These findings are regarded as presumptive evidence of inferior mesenteric artery obstruction at the mid third of the left ureter and exploration will be carried out if there is stone formation, further pyelonephritis or increasing obstruction.

Discussion

The operative technique for bringing the left ureter to the right iliac fossa during these ileac diversions consisted of blunt dissection in the root of the mesocolon dorsal to the inferior mesenteric artery and ventral to the great vessels. The left ureter was then pulled through this opening which was large enough to allow the ureter to lie in a gentle curve from the left renal pelvis to the right iliac fossa.

The left ureter also follows an anterior course as it passes from the retroperitoneum of the left side forwards to its anastomosis with the proximal end of a short ileac loop in the lower right abdomen. Along this course the left ureter hooks under the inferior mesenteric artery. The treatment in our cases with obstruction by the inferior mesenteric artrey was to ligate and divide the artery after occlusion by a bulldog clamp for 10 minutes to insure adequate anastomatic blood supply to

the descending and sigmoid colon.

In bedridden paraplegics and multiple sclerosis patients the inferior mesenteric artery follows a posterior course to the sigmoid colon which lies dependently against the postabdominal wall. This posterior course of the inferior mesenteric artery and the anterior course of the left ureter could accentuate the hooking of the ureter under th artery which would be avoided if the left uret was brought through the mesocolon ventral to th inferior mesenteric artery. One cause for ureter obstruction following ileac diversion would b eliminated.

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It's the Law

General Practitioner's Duty To Seek Con ultation

A man was taken to a hospital emergency room because he was nervous and shaky. His wife stated he had been drinking and had been having hallucinations.

The patient was examined by a general practitioner who was not his regular family physician. This physician made a diagnosis of "alcoholism DT's." He was hospitalized.

By the next day, the patient was restless and still having hallucinations. When the physician saw him at 8:30 A.M., the man was in a comatose condition, and by 3:00 P.M., he had not eaten. The physician ordered an intravenous feeding and called for neurosurgical consultation. The patient died at midnight.

The autopsy revealed that the patient had had a subdural hematoma for approximately 48 hours.

The patient's widow and children sued the general practitioner and the hospital claiming that the physician negligently failed to obtain appropriate consultation.

The jury found that the physician was not negligent in failing to call a specialist on initial examination. The appeal court noted that there was no evidence that the physician had violated any standard of care. They further noted that a general practitioner is not required to consult a specialist on every conceivable complication that might arise.

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Chascp v. Providence Memorial Hospital, 476 S.W. 2d 385 (Tex. Ct. of Civil App., January 12, 1972, The Citation, 25:6, July, 1972.

Tetanus in Minnesota

MARK V. DAHL, M.D.

TETANUS IS A rare, often fatal disease resulting from infection with *Clostridium tetani*. This bacterium is present in the soil,[1,2] and is occasionally cultured from the gastrointestinal tracts of healthy people.[3] When present in a suitable anaerobic environment such as necrotic tissue, the organism produces an exotoxin which binds to neural tissue and causes a progressive disinhibition of nerve impulses resulting in the clinical disease tetanus.[4]

The purpose of this retrospective study is to review the experience with tetanus at the University of Minnesota Hospital from 1955 to 1971. Particular attention is given to events leading to death and influencing mortality in these patients.

Methods

Fifty-six patients with tetanus were admitted to the University of Minnesota Hospital between January 1, 1955 and June 30, 1971. The diagnosis of tetanus was questionable in three patients (all non-fatal), and these patients were excluded from the study. The clinical diagnosis of tetanus was well-established in the remaining 53 patients. Medical records were reviewed and clinical data tabulated. Autopsy reports of 17 patients who died were also reviewed.

Results

Thirty-eight patients (72%) lived outside a 50-mile radius of Minneapolis-St. Paul. Only four patients (8%) were residents of these cities proper. All patients were white and the males outnumbered females 37 to 16 (2.3:1). The patients ranged in age from one week to 82 years with a mean age of 43. Two patients were less than one month old. The distribution of age groups is depicted in Figure 1. Thirty-six patients (68%) developed tetanus during the six summer months from April through September (Figure 2).

Thirty-two patients (60%) reported no previous immunization against tetanus. Of these, six had received an initial tetanus toxoid immunization after the injury which preceded development of tetanus. Ten patients (19%) reported immuniza-

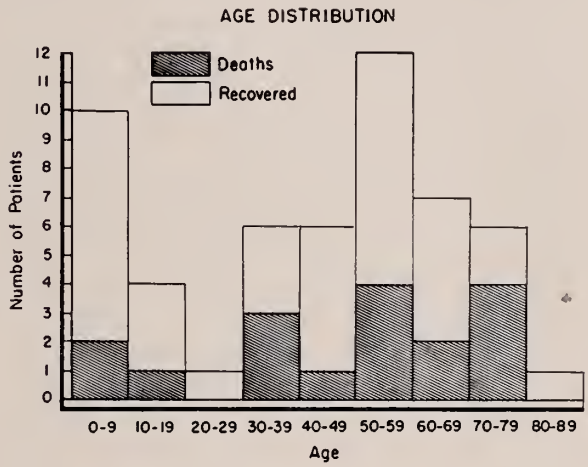


Figure 1

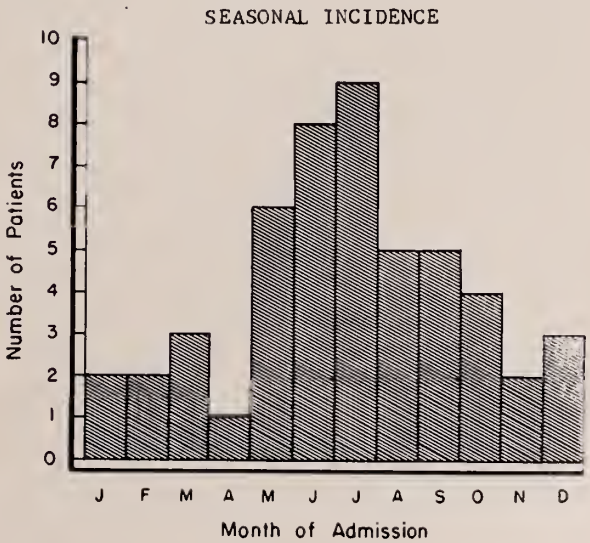


Figure 2

From the Division of Infectious Diseases, Department of Medicine, University Hospitals, Minneapolis, Minnesota.
Carried out during senior year at the University of Minnesota Medical School.
Present Address: Department of Dermatology, University of California Hospitals, San Francisco, California.
See editorial, page 817.

tions against tetanus prior to injury. The immunization status was unknown in 11 patients (21%).

A site of infection was noted or reported by all but three patients (94%). Farm machinery produced 12 of the precipitating injuries (24%), and puncture wounds accounted for 12 others (24%). Five puncture wounds resulted from rusty nails. Infection with *C. tetani* also resulted from crush injuries, gunshot wounds, incomplete abortions, burns, and chronic leg ulcers. Operations apparently introduced infection in two patients. No patients were known narcotic addicts.

In 26 patients (50%), the site of injury was the upper extremity. Four of eight patients (50%) died with infection sites on the head or trunk, whereas 12 of 32 patients (38%) died from initial infection on an extremity.

The incubation period between inciting event and onset of symptoms was three to 35 days with a mean of 10 days and a median of seven days. It was not possible to determine the incubation period in eight patients. One of 13 patients (8%) with an incubation period longer than 10 days eventually died during hospitalization. In contrast, 10 of 25 patients (40%) with incubation periods less than seven days died during the course of the disease.

The mean onset time between first symptom and first convulsion was 48 hours among 39 patients who developed convulsions. Most of these had been treated with various tranquilizing drugs prior to the first convulsion. Five of nine patients (56%) with onset times of 36 hours or less eventually died. Two of 12 patients (17%) with onset periods longer than 60 hours died.

Inability to open mouth was the most frequently chief complaint (20 patients). Difficulty swallowing (8), stiff neck (8), and painful neck (7) were other common chief complaints. Other patients reported stiff legs, back pain or stiffness, jaw pain, jerking of an arm, gagging, abdominal cramping, and various sensations in the throat as the initial symptom. There was no relationship between chief complaint and mortality.

Clostridium tetani was grown from culture of infected wounds of seven patients (13%). Three of these (43%) eventually died during hospitalization. An extremity or digit was amputated from 16 patients of whom five eventually died during the course of their disease (31%). Tracheotomy was performed on 40 patients. All 17 patients who died had previously undergone tracheotomy.

All 53 patients received tetanus antitoxin prior to or during hospitalization. There were three deaths among seven patients who received human tetanus antitoxin, and 14 deaths among 46 patients who received horse antitoxin. There was no relation of mortality to either initial dose or total dose of tetanus antitoxin. The mortality rate of patients who first received tetanus antitoxin prior to the onset of convulsions (five of 12) did not differ significantly from the mortality rate of patients who first received tetanus antitoxin at or after onset of convulsions (12 of 41). Gavage or gastrostomy feedings were given to 32 patients of whom 11 died, (34%).

Body temperatures above 100°F were recorded during hospitalization in all 53 patients. The degree of elevation or pattern of body temperature over time reflected convulsive activity or complicating infection but did not appear to have prognostic significance. Characteristically, the blood pressure fluctuated widely, but its degree or pattern did not indicate impending death except to the extent a low blood pressure indicated shock. Various laboratory tests including analysis of the cerebrospinal fluid also had no prognostic significance.

Numerous drugs were administered. Antibiotics were given to all 53 patients. Major muscle relaxants such as curare, gallamine, and succinyl choline were given to 24 patients with 12 subsequent deaths (50%). Minor muscle relaxants such as methocarbamol were used in four patients. Forty patients received barbiturates, 39 patients received phenothiazine tranquilizers, and 17 patients received minor tranquilizers such as meprobamate, diazepam, and chlordiazepoxide. Six patients were treated with diazepam and two of these died (33%). Non-barbiturate sedatives such as paraldehyde and chloralhydrate were administered to 12 patients, and magnesium sulphate was administered to five patients.

Autopsies were performed on all 17 patients who died. Seven patients (41%) died within five days and 12 patients (71%) died within 10 days after admission to the hospital. One patient died as late as 28 days after admission. Bronchopneumonia was noted at autopsy in eight patients, and atelectasis in seven. Pulmonary embolism was present in six patients (35%). Other findings at

autopsy included septicemia (5), gastrointestinal ulceration (4), myocardial hemorrhage, necrosis, or infarction (3), peritonitis (1), pyelonephritis (1), and acute supperative cholecystitis (1).

Comments

The 17 deaths in this series of 53 patients with tetanus represents a mortality rate of 32%. This approximates the death rate currently being reported by other institutions.[5-10] The mortality of tetanus has decreased since World War II.[11-13] This is attributable primarily to the role of antibiotics in both chemical elimination of the *Clostridium tetani* organism from the infected wound, and control of superinfections especially pneumonia. New anesthetic and sedating techniques and medications probably also contribute to this world-wide reduction of mortality from tetanus.

Most patients were males from rural areas. Farmers are particularly likely to sustain injuries with soil-contaminated objects. Contact of a wound with soil increases the likelihood of infection with *C. tetani*.[1,3] More than one-fourth of infecting wounds were from farm equipment. Differences of immunization practices may also account for the apparent predisposition of rural populations to tetanus. The extent to which the University of Minnesota's role as a referral center acts on selection of patients is not known. Tetanus was treated between 1955 and 1971 in at least four other Minnesota hospitals.

Most tetanus occurred in the summer (Figure 2). The paucity of cases during the winter months probably reflects both the agricultural habits of the state, and the severity of Minnesota winters. Wounds by soil-contaminated objects would be less common in winter.

The age of patients ranged from one week to 82 years (Figure 1). Immunization status is most likely to be deficient in the pediatric and over-fifty age groups, and most patients were included in one of these two groups. Two patients had neonatal tetanus. The umbilical stump was grossly infected in one of these infants. The mortality rate was approximately equal in all age groups. Others have noted higher mortality rates in small children and persons over age 60 years.[9,13]

The frequency of tetanus treated at the University of Minnesota decreased during the 16 years included in the study. Only four patients were treated for tetanus from 1967 to 1971. The number of admissions to the University of Minnesota Hospital during the 16 years remained relatively constant at about 15,000 patients each year.

A majority of patients reported they had never received even a single immunization against tetanus. Documented cases of tetanus in patients previously immunized are rare.[14] Ten of 43 patients in this study reported prior immunization. In many patients, the last immunization had been given many years previously. Protection by immunization requires periodic booster injections. History may not always be reliable in accessing immunization status.

The well-known relationship between the mortality rate and the incubation period is demonstrated in this study. The shorter the period between injury and development of symptoms, the higher the mortality rate.[1,5,7-9,13,15] This may be the best indicator of prognosis in any given patient.

There is another well-known relationship between the onset period and the mortality rate. The onset period is the interval of time between appearance of the first symptom and the initial convulsion. A prolonged onset period indicates a more favorable prognosis.[1,5,7-9,13,15] This relationship is sometimes masked by difficulty defining a convulsion in some patients, the incideous onset of the initial symptom, and the use of numerous drugs which delay or prevent onset of convulsions. However, the relationship is valid, and is demonstrated in this series.

Cultures from most patients were negative for *C. tetani*. Perlstein similarly reported only four positive cultures in his series of 59 patients.[15] The diagnosis of tetanus is a clinical diagnosis, and is not dependent on finding the etiologic organism in culture.

Forty patients had undergone tracheostomy. Elective tracheostomy is performed on all patients with pharyngeal or laryngeal involvement. A major cause of death in untreated tetanus is asphyxia from spasm of the glottis, diaphragm, or intercostal muscles.[16,17] Spasm of the glottis was not a factor in death of any patient in this series, since all patients who died had undergone tracheostomy.

Treatment

Treatment must be tailored to each individual patient. Probably no single therapeutic regime is suitable in all respects in any given patient.

At the University of Minnesota, the anesthesiology department has prime responsibility for management of the total paralysis regime and overall supervision of treatment. The departments of

medicine and pediatrics function to maintain nutrition and electrolyte balance, and prevent and treat complications. Surgeons perform debridement, tracheostomy, gastrostomy and follow-up care of the infected wound. Neurology follows the patient in a consultative role. Specially trained nurses are assigned to deliver continuous care on a 24-hour-a-day basis. Nurses who previously had cared for patients with tetanus are assigned when possible.

Treatment is initially directed at removing the source of toxin, controlling spasms, and preventing respiratory arrest.[16] Initially 1000-2000 units of human tetanus immune globulin are administered intramuscularly to neutralize unbound toxin. Christensen has advocated injection of small amounts into multiple sites to speed absorption since once toxin is fixed to nervous tissue it can not be neutralized.[18]

Tracheostomy is performed early in the course of hospitalization on any patient where pharyngeal or laryngeal involvement is present or anticipated. A double-cuffed tracheostomy tube allows optimum care. The wound is amputated or debrided widely. When debridement is performed, the wound is totally excised if possible. The deep fascia, any involved muscle, and at least a two centimeter margin of skin around the wound is also excised. The wound is allowed to heal initially by secondary intention although it may be closed at a later date if indicated.[18] Dressings are applied lightly and initially kept wet with 3% aqueous hydrogen peroxide or a 1:4000 aqueous solution of potassium permanganate.

Penicillin is the drug of choice to eliminate the clostridium organism chemically. Ten million units of aqueous penicillin G are administered by continuous intravenous drip during the first 24 hours.[18] Thereafter, one million units of procaine penicillin are administered daily intramuscularly for six to 10 days.[14] Kanamycin streptomycin, or tetracycline may be administered to aid elimination of synergistic gram-negative bacteria.

Recently intravenous and oral diazepam has been used both as a sedative and muscle relaxant.[19] An initial intravenous injection of five mgm is administered, and increased five mgm every two hours until convulsions are controlled or limits of toxicity are reached. Up to three mgm/kilogram/day is occasionally used. Femi-Pearse has treated one patient with 40 mgm/kilogram/day.[19] The dose of diazepam is titered by clinical parameters. Proper control is obtained when the temperature remains stable and convulsions occur only with stimulation. At this dose range, the cough reflex is still active and assists in clearing pulmonary secretions. If additional medication is needed, gallamine 20-60 mgm every twenty minutes may be given intravenously. In these patients, intermittent positive pressure ventilation is necessary. Oversedation is a definite hazard.

Convulsions are occasionally stimulated by rectal or bladder fullness although viscerally stimulated convulsions are less common when diazepam is used. An indwelling bladder catheter may itself precipitate convulsions. In these cases, intermittent catheterization or cystotomy may be performed. If an indwelling catheter is used, it is cleansed daily with alcohol or disinfectants, and changed at least every two weeks. An antibiotic ointment is applied to the urethral meatus, and the urine acidified if feasible to minimize infection. Tap water enemas reduce visceral stimulation from the rectum.

One thousand units of human tetanus immune globulin are administered daily for four or five days by intramuscular injection. Equine tetanus antitoxin is no longer used.

The central venous pressure and urine output and specific gravity aid management of fluids and electrolytes, and allow early diagnosis of shock should it occur. The patient may require large amounts of fluids to replace excessive loss from perspiration during convulsions. A cooling blanket may be necessary to reduce fever from convulsions or medullary intoxication. Gavage or gastrostomy feedings do not appear to increase mortality in our experience, and may be used after the acute phase. Care must be taken to avoid vomiting and aspiration from overfilling the stomach. The gastrostomy catheter may be used to decompress the stomach if distension is noted. Because stress ulcers are common, frequent administration of antacids is recommended. The legs are wrapped to the upper thighs with six-inch-wide elastic bandages. Each day the legs are unwrapped and examined for erythema and edema indicating thrombophlebitis.

Vigorous tracheal aspiration under sterile conditions and proper tracheostomy care are essential if a complete paralysis regimen is used. Serial daily cultures of tracheal aspirate and urine are helpful as guides to proper selection of antibiotics when lung or urinary tract infection occurs. In-

ceting organisms are usually klebsiella, aero-bacter, pseudomonas, and staphlococci.[18] Arterial blood gas determinations are usually necessary for proper regulation of positive pressure ventilation when used.

Hematocrit and examination of stool for occult blood are performed frequently. Anemia develops in nearly every patient with severe tetanus and may require transfusion. The anemia may develop from peptic ulceration, but more often is probably the result of toxic depression of the bone marrow. During recovery, active hematopoiesis is usually resumed.

If a total paralysis regimen with gallamine is used, the eyelids are kept closed. Methylcellulose eyedrops are instilled three times daily in each eye. If conjuctivitis develops, neosporin ophthalmic ointment is usually preferred pending results of culture.[14]

Prophylactic measures are taken to prevent contractures and decubitus ulcers. Bedboards and footboards are helpful. The extremities are passively brought through full range of motion at least once daily. Decubitus ulcers may be prevented by changing position of the patient each hour. Sheepskins or alternating pressure mattresses relieve ischemia of the skin and reduce shearing forces of bedsheets on pressure areas. The skin is kept dry as well as clean. Frequent inspection of skin especially over sacrum, trochanters, ischial tuberosities, and calcanea is important.

Clinical tetanus does not confer immunity. Active immunization with tetanus toxoid is begun during the recovery phase.

No patient received hyperbaric oxygen therapy. Laboratory and clinical studies indicate that treatment with hyperbaric oxygen is not warranted.[20,21]

Recently Saunders advocated intravenous administration of betamethasone. Three hundred sixty-two infants with neonatal tetanus received 24 to 32 mgm daily with a reduction of mortality from 61% to 37%.[22] Betamethasone has not been used to treat tetanus at the University of Minnesota Hospital.

Kerr used anticoagulants to minimize the possibility of pulmonary embolism.[23] Pulmonary embolism was present at autopsy in six patients in this series.

Regardless of therapy, tetanus will appear to progress for four to seven days. Because the half-life of tetanus toxin bound to neural tissues is long, the patient will usually remain stable for two or three weeks before improvement is noted.

It is apparent from autopsy data reviewed in this study that serious complications are present in most of the patients with tetanus who die. Prevention of complications and therapeutic advances may allow further reductions of the mortality rate. The major complications are infections such as: pneumonia, septicemia, peritonitis, cholycystitis, and pyelonephritis. Pulmonary embolism, myocardial injury, and stress ulcer occur frequently.

Direct causes of death from tetanus include: asphyxia, exhaustion, and medullary failure.[17] Firor suggested that tetanus toxin or some metabolite might have a direct effect on the medulla.[24] Baker noted swelling and perinuclear chromatolysis of nerve cells of the cortex and brain stem, and perivascular demyelination and gliosis near the nucleus of the vagus nerve in a series of patients who died from tetanus.[3,25] Montgomery also concluded that direct action of tetanus toxin or some metabolite on the medulla may be responsible for death of some patients.[6] Death from tetanus may result from tetanus itself as well as from second complications. However, medullary failure may be reversible if efficient ventilation can be maintained.[26]

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19-26. See page 806.

Respiratory Distress Syndrome

Preventive Aspects

MARTHA BURKE-STRICKLAND, M.D.

PREVENTION OF THE respiratory distress syndrome depends first on preventing prematurity and second on perinatal intensive care of all infants at risk. Such intensive care should begin in the labor room and continue from the delivery room to the newborn intensive care unit.[1]

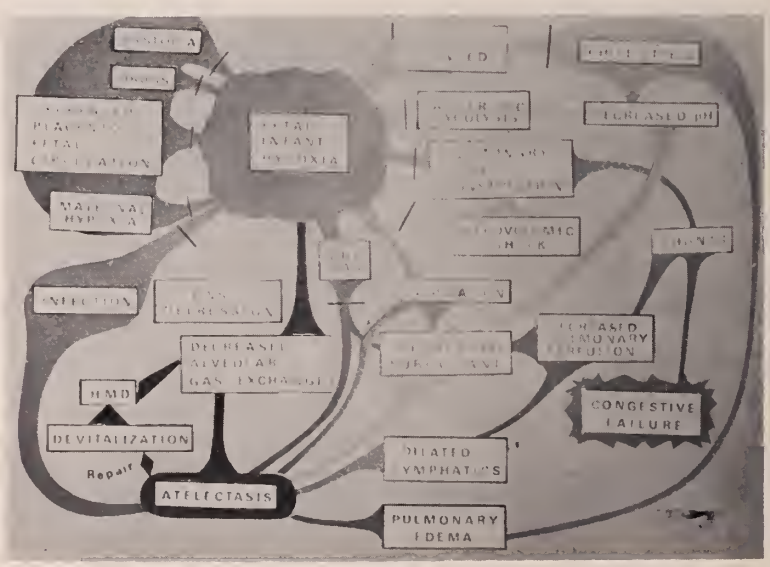
The obstetrician, pediatrician, and anesthesiologist should work together as a team, but the primary responsibility should be the pediatrician's. He should be trained for fulfilling this role on the team. The Table lists some of the conditions known to produce infants at risk. When one of these conditions is identified in an expectant mother her physician should plan for the baby to be delivered in a perinatal center.[2,3] The pediatrician should be informed and kept posted on the progress of the pregnancy. When labor begins all members of the perinatal team should be notified.

The pediatrician should keep informed concerning the infant's condition during labor, be present at the delivery and be responsible for resuscitation of the infant immediately after delivery.

The Figure is a graphic representation of the production and consequences of fetal or neonatal hypoxia. The dotted lines crossing pathways of involvement represent points at which intervention by the team should improve the outcome for the infant.

Presented at the Minnesota Chapter of the American Academy of Pediatrics September 24, 1970.

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Figure

Pre-Delivery Concerns for the Fetus

Maternal Hypoxia

Maternal hypoxia causes fetal hypoxia. As long as the materno-fetal circulation is intact, the fetal hypoxia can be alleviated by giving the mother 100% oxygen.[5,6]

Most anesthetic and sedative drugs cross the placenta. Some i.e., magnesium sulfate, barbiturates, carbocaine and Nisental have a direct central-nervous-system depressing effect on the fetus.[7,8,9] Bradycardia may be noted before delivery but acid-base balance is usually maintained until the cord is cut. In some infants a mild to moderate fetal acidosis may develop.[10,11] Infants with a diminished respiratory drive may not breath enough to maintain a normal pH, pO_2, and pCO_2. Anesthesia and sedative drugs should not be used unless absolutely necessary. When they must be used, then anticipatory assistance of ventilation must be given immediately after delivery and continued until the infant breathes well on his own. Concomitant monitoring of pH and blood gases is necessary.

On rare occasions, magnesium sulfate levels in the infant may be high enough to require exchange transfusions.[12,13] To reduce the assisted ventilation time required for an infant depressed by Nisental or other narcotics, 0.25 mg. Lorfan may be given.[9]

Decreased Placento-Fetal Circulation

Factors which decrease placental circulation affect the quality of the blood supply to the fetus. Monitoring of the fetus and anticipatory care are mandatory in all abnormal circumstances.

Maternal hypertension (toxemia) causes arteriolar alteration with decreased placental perfusion.[14,15] Uncontrolled for long periods of time, it results not only in hypoxia, but in diminished transfer of nutrients to the fetus. The resulting small-for-dates infant with chronic hypoxia is more vulnerable to the extra stress of delivery.[16,17] Intensive prenatal care and control of hypertension markedly reduce the infant morbidity and mortality.[18]

Maternal hypotension is usually an acute episode from blood loss, dehydration, infection, or local anesthestic agents.[8] Effective treatment depends on re-expansion of maternal circulating volume. Lowering the head and elevating the limbs may be helpful when the problem arises with spinal anesthesia.[8,9] Vasoconstrictors may improve the mother's blood pressure, but they may worsen placental profusion.[19]

Compression of the pelvic vessels can occur with prolonged positioning of the mother on her back during labor and delivery. This can be minimized by repositioning the mother and shortening the time she is on her back.[8,20] When compression of the vessels cannot be circumvented, then fetal hypovolemia and hypoxia should be anticipated and corrected immediately upon delivery.

Abruption of the placenta results in interruption of maternal-fetal exchange. The hemorrhage brings about hypovolemia and anemia and may add the extra complication of defibrination syndrome.[21] Base line fibrinogen level and platelet count should be obtained on the infant as soon as it is born, and these should be re-assayed every six hours for 24 hours or at any time the infant is symptomatic. When the prothrombin-time is greater than 2½ times the control, partial thromboplastin time greater than two minutes, fibrinogen level less than 0.05%, platelets less than 75,000, the infant should be given intravenous heparin 100 units/kg. Clotting studies should be repeated every four hours and additional doses of heparin should be continued every four hours (50u/kg) until factors are back to normal—usually within 48 hours.

Compression of the umbilical cord may result from knots in the cord, a nuchal cord or entrapment of the cord between fetal parts and the pelvis or the contracting uterus. Compression of the umbilical cord usually produces an acute hypoxia in the fetus from which the fetus recovers promptly with stimulation and assisted ventilation unless a prolonged second stage allows chronic hypoxia to develop.[8,22] Forceps delivery or interruption of labor may be indicated.[17]

Hypertonicity of the uterus during labor is best detected by monitoring of uterine contractions

TABLE

Conditions Associated with High Risk for the Infant

Habitual perinatal death	Fetal bradycardia
Maternal diabetes	Multiple births
Pre-eclampsia	Placenta previa
Evidence for intrauterine growth retardation	Cephalo-pelvic disproportion
Elderly primipara	Breech presentation
Rh sensitization	Abruptio placenta
Maternal narcotic addiction	C-section
Prolonged gestation	Polyhydramnios
Prolonged rupture of membranes	Oligohydramnios
Last trimester infection	Maternal thyrotoxicosis
	Rapid succession and pregnancies

with an intrauterine catheter and transducer.[23] Problems created by hypertonicity can be relieved by stopping labor and doing an emergency C-section.

Fetal Monitoring

Monitoring is used to follow the condition or response of the fetus to stressful intrauterine conditions. Several methods are useful.

Amnioscopy

Whenever chronic hypoxia is suspected in the last six weeks of pregnancy, direct examination of the amniotic fluid may be done as often as every other day. Variation from the normal clear or milky fluid may indicate imminent danger to the fetus.[24]

Amniocentesis

Direct samples of amniotic fluid may be obtained as early as 20 weeks gestation and thereafter to monitor excess bilirubin metabolites resulting from Rh sensitization. Measurement of estriol excretion in the amniotic fluid and analysis for creatinine levels may be used to determine gestational age for elective induction of labor or C-section.[25] Amniotic fluid cell analysis for inborn errors of metabolism and for chromosomal abnormalities is still used only as a research tool.

Since this was presented the use of Amniocentesis to determine lecithin—sphingomyelin ratios in the amniotic fluid has become very important in assessing fetal age. As lungs mature in utero, more lecithin is produced. When the lungs are mature enough to support life with less risk of respiratory distress syndrome the ratio is greater than 1.5 to 1. The infant will be safer if the ratio is 2:1. This is helpful in setting a time for elective C-Sections to insure that the infant is not delivered prematurely.*

Fetal Heart Rate

In assessing fetal heart rate, patterns are more important than range. Deviation from a base line and timing in relation to uterine contraction are important. Therefore, fetal heart rate and uterine contractions should be recorded simultaneously.

Three major patterns have been described: (a) early deceleration (Hon) or Type I dips (Caldeyro-Barcia) in which an early onset of bradycardia coincides with beginning uterine contractions. This type is thought to be due to head compression. No fetal pH or blood gas changes occur. The effect is altered by atropine.

(b) Late deceleration (Hon) or Type II dips (Caldeyro-Barcia) in which a bradycardia begins late in the uterine contraction. It is only partially modified by atropine, is accompanied by fetal acidosis, and is thought to be due to utero-placental insufficiency. If Type II dips appear and persist, it is recommended that labor be interrupted and an emergency C-section performed.

(c) Variable deceleration (Hon) occurs at variable times during uterine contractions. This is thought to be caused by umbilical cord compression. It is markedly altered by changes in maternal position or fetal manipulation; it is not associated with fetal acidosis unless the episodes of deceleration are frequent and prolonged.[22,27]

Scalp Blood Sampling

As soon as cervical dilatation and rupture of the membranes permit access to the fetal scalp, blood sampling can begin for the fetus who shows other signs of distress.[24,28] Capillary blood from the scalp has been proved to be a reliable sampling for determining status of the fetus.[28,29] A fetal pH less than 7.25 is generally accepted as a danger signal. pH is reliable as an indicator of fetal distress only when considered in context with other maternal-fetal parameters under observation.

Passage of meconium, type II dips, and fetal acidosis represent a level of hypoxia that demands intervention for the fetus.[22,24,27,30] The type of intervention will depend on the stage of labor and on the presenting conditions causing the distress.

Post-Delivery Infant Care

For anticipatory care of the newborn at risk, the pediatrician should be on hand in the delivery room when the delivery starts. All instruments and supplies for handling any emergency should be checked and ready for instant use even though they may not be used, because the time saved when they are needed may make the difference between a baby who survives adequately and one who survives with neurological damage.

The basic concepts of care can be summarized as follows:

Avoid "chill stress" of the infant.

Establish effective ventilation within one minute if possible. If no spontaneous respiratory effort is made by the baby, do not wait for the one-minute Apgar to tell you the infant needs help. Clear the airway and assist breathing by mask. Continue for 30 seconds if this is ventilating the chest, but if

*Whitfield, C R, Chan, W H, Sproule, W B & Stewart, A D, Amniotic Fluid Lecithin: Sphingomyelin Ratio and Fetal Lung Development. Brit Med J 303:85, 1972.

here are still no spontaneous respiratory movements, then intubate, use suction, and continue assistance with a mechanical ventilator as long as needed.

Correct metabolic acidosis immediately. Increasing the pO_2 and correcting the pH will relieve the pulmonary vasoconstriction.[31,32,33] Early correction of pH may also protect surfactant generation in the alveoli.[34] This can be done through the umbilical vein catheter by administration of a few cubic centimeters of solution containing 1 mEq/cc of $NaHCO_3$. One mEq/kg is given over a three to five-minute period. Further bicarbonate therapy is based on response of the infant and reported values for specimens drawn.

Begin therapy for hypovolemic shock[35] if the central venous pressure is less than 3 cm. H_2O, and the blood pressure is less than 20 mmHg. Give isotonic serum albumin intravenously at the rate of one gram/kg. Keep in mind that the sodium given for acidosis also acts as a volume expander; it has an osmotic potential for 7.2 cc water.[36] As the circulating osmolality is acutely increased, water will be drawn into the circulation in a matter of minutes. Redistribution of ions across the tissues may take several hours.

Keep handling to a minimum. The autonomic nervous system of the infant is in a state of siege. This is true of any newborn trying to adjust to an input of stimuli from many new sources. The fewer unnecessary stimuli he has to cope with, the sooner stability will be reached.[37,38] Every extra handling increases the energy demand for oxygen and if the infant's lungs are already behind in meeting need, extra calls for O_2 that can't be delivered only increase the metabolic deficit.

Supply the infant with energy. The high-risk infant may already have exhausted glycogen stores by the time delivery is completed. Continuing intravenous therapy with 10% glucose solution minimizes the chance of hypoglycemic shock as well as respiratory lag from fatigue.[39]

Use only humidified gases for assisted ventilation. Use of oxygen enriched air (30-35%) will suffice most of the time. Do not use 100% O_2 as it may actually "burn" the lungs as well as increase atelectasis; 100% O_2 displaces the inert N_2 gas in the residual functional volume of the lung. When the O_2 is absorbed into the perfusing circulation, the alveoli collapse at the end of expiration.[41]

Look for heart failure, and support as necessary although not every baby with hypoxia nor every baby with respiratory distress syndrome will have heart failure. A baby with a gallop rhythm and a liver down to the pelvic brim is probably in failure. One half the digitalizing dose of Lanoxin (0.04 mg/kg.) intravenously, will bring improvement within fifteen minutes. Cardiac failure does not preclude the use of $NaHCO_3$ for correction of acidosis, but the bicarbonate solution must be given more cautiously. The infant in failure will usually have a high central venous pressure (greater than 10cm H_2O) and variable blood pressure. Until the heart failure is corrected, no expanding fluids are needed, so the intravenous canula is kept open at 0.5 cc/hr for medications only. This degree of control can be achieved with a Harvard constant infusion pump.

Move with dispatch. Do the before-mentioned things in the delivery room. Time is of the essence if these therapeutic measures are to be preventive.

Transport only after stabilized. When the initial support measures are completed and the infant begins to stabilize, he may then be transported to an intensive care nursery for continued monitoring and therapy. Transport should be accomplished without disruption of the measures already described. A skilled attendant must accompany the infant whether the trip is to a unit across the hall or across town.

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15-40. See page 850.

Pancreatic Scanning

Blind Review by Multiple Observers

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MANY RECENT COMMUNICATIONS express some ambivalence about the value of pancreatic scanning. The initial enthusiasm in the early 1960's was modified by the later experience of physicians who found that pancreatic images were difficult to recognize and sometimes nonexistent, even when the pancreas subsequently was found to be normal.[1-11] Review of many reports suggests that the scan diagnosis often was made with knowledge of significant clinical information. Photographs emphasize classic examples.[5,8,10,12] The physician is most in need of help when there are no positive findings and a decision for or against surgical exploration must be made. There are few reports of blind reviews of pancreatic scans.[2,8] Therefore we undertook a study of scan interpretation by five observers with varied backgrounds and interests. The accuracy of each observer in detecting the presence of pancreatic disease and the agreement among them were assessed.

Material and Methods

Five observers reviewed selenium-75 scans of the pancreas in 71 patients, without prior knowledge of other findings in the cases. The scanning was performed by conventional techniques[13,14] after injection of 200 μCi of selenomethionine from two suppliers (Squibb Laboratories and Amersham/Searle). Sixty-seven ^{131}I-labeled Rose Bengal liver scans were available, permitting electronic subtraction in 32 and visual subtraction in all.[13,15,16] Cancer or pancreatitis was subsequently confirmed in 19 of 44 abdominal explorations or autopsies. A clinical diagnosis of normal pancreas was made in 21 cases and mild pancreatitis, in six. Adequate follow-up data were obtained in most of the normal patients to eliminate the possibility of carcinoma.

The observers included a gastroenterologist, three laboratory physicians, and a nuclear medicine technologist. All had experience with scanning procedures. The coded scans were presented randomly. The pancreatic image was judged to be indeterminate, normal, absent, or abnormal, based on decrease in count rate, absence of an image, or apparent filling defects. The correctness of the response was determined without regard to location of the lesion within the pancreas, since precise localization is beyond the limits of this technique in most instances. Each observer recorded his findings for the 32 electronically sub-

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TABLE 1
Representative Responses*

Scan	Subtraction Technique	Observer Response 1	2	3	4	5
1	Visual	I	I	I	N	N
2	Visual	N	I	D	D	N
	Electronic	N	I	I	I	N
3	Visual	N	I	A	H	N
	Electronic	N	D,H	A	H	N
4	Visual	N	N	N	N	N
5	Visual	A	A	A	A	A
6	Visual	I	I	A	I	N
	Electronic	D,H	A	D	D,H	N

*Code: N = normal; D = decreased count rate; H = holes; A = absent; I = indeterminate.

TABLE 2
Agreement of Scan Assessment With Final or Correct Diagnosis

Subtraction Technique	% Agreement, by Observer 1	2	3	4	5
All Scans					
Visual	68	43	56	40	62
Electronic	83	46	67	40	62
Scans with tissue confirmation					
Visual	71	44	57	37	62
Electronic	90	53	25	47	71

TABLE 3
Correlation of Scan Findings with Proved Findings

Observers (no.)	Proved Findings (no.) Normal Pancreas	Abnormal Pancreas
"Normal" on scan		
5	4	0
4	6	0
3	13	2
"Absent" on scan		
5	3	2
4	5	5
3	3	3

acted scans.

Results

There was considerable variation among observers. Table 1 shows several representative patterns. Each observer consistently tended to overinterpret or underinterpret abnormalities. Zero to 17% of the unsubtracted scans and 0 to 3% of the subtracted scans were recorded as indeterminate. Agreement with the final or correct diagnosis ranged from 68% for observer 1 to 40% for observer 4 with scans read by visual subtraction (Table 2). The agreement was not significantly better with electronic subtraction scan results in the entire group were the same as in the surgically proved cases.

A well-defined outline (Figures 1 and 2) recognized by three or more observers was highly predictive of normality (Table 3). Other positive correlations could not be defined. Although an absent pancreas (Figures 3 and 4) was taken as evidence of an abnormality in calculating the accuracy of response, the finding of an absent pancreas has no predictive value and such a scan cannot be interpreted.

Discussion

Pancreatic scans are imprecise. Some of the scans were technically superior to others for reasons which were not evident; the same methods were used throughout.

There was considerable variation among observers in our study. Observer 1 tended to view wide differences in shape and density of the pancreas as normal; this probably accounts for his greater accuracy. Observer 4 consistently over-reported abnormalities. Of interest is the accuracy of observer 5 who chose not to record any scans as indeterminate. Had this been done, with the elimination of some borderline scans (Figures 5, 6 and 7), his results, and indeed all results, would have been better. Acceptance of this limitation will decrease the element of guesswork.

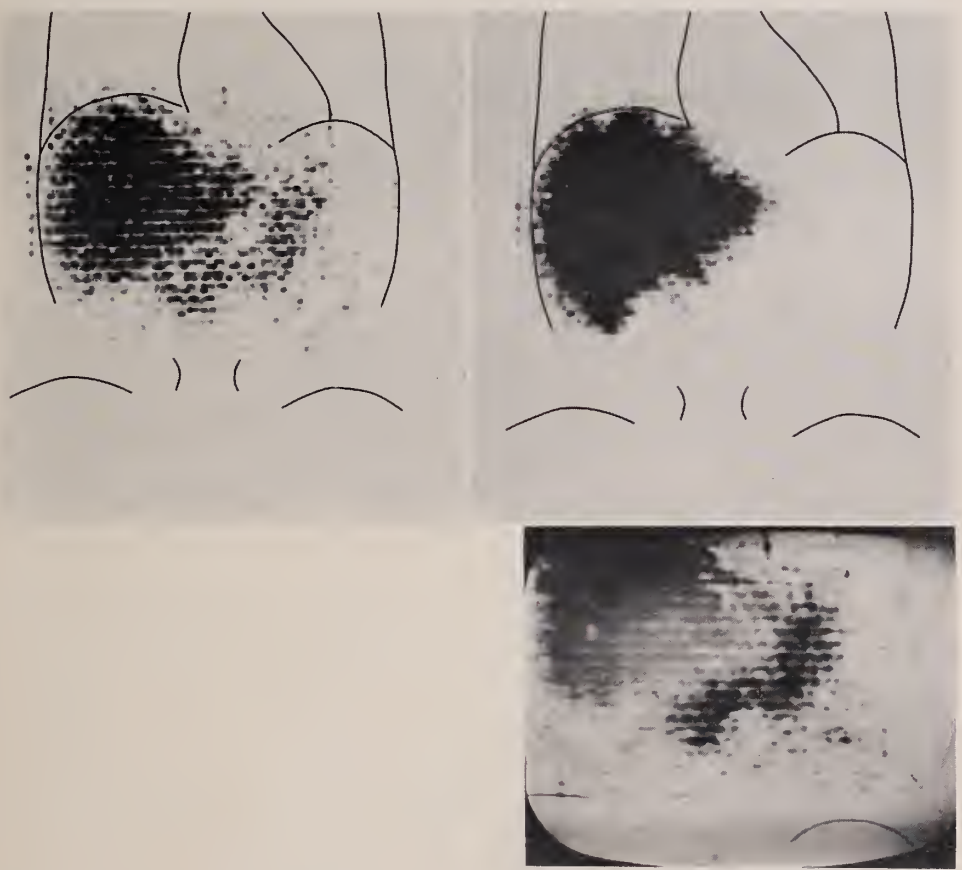


Fig. 1—*Upper,* Classically normal isotope pancreatic scans. Organ is sigmoid in shape, separate from liver. *Left,* Selenomethionine. (From McGill DB, Tauxe WN: Radioisotope scanning of the pancreas. Med Clin North Am 54:881-888, 1970. By permission of W. B. Saunders Company.) *Right,* ^{131}I-labeled Rose Bengal, *Lower,* Subtraction analysis is somewhat superfluous here but demonstrates technique.

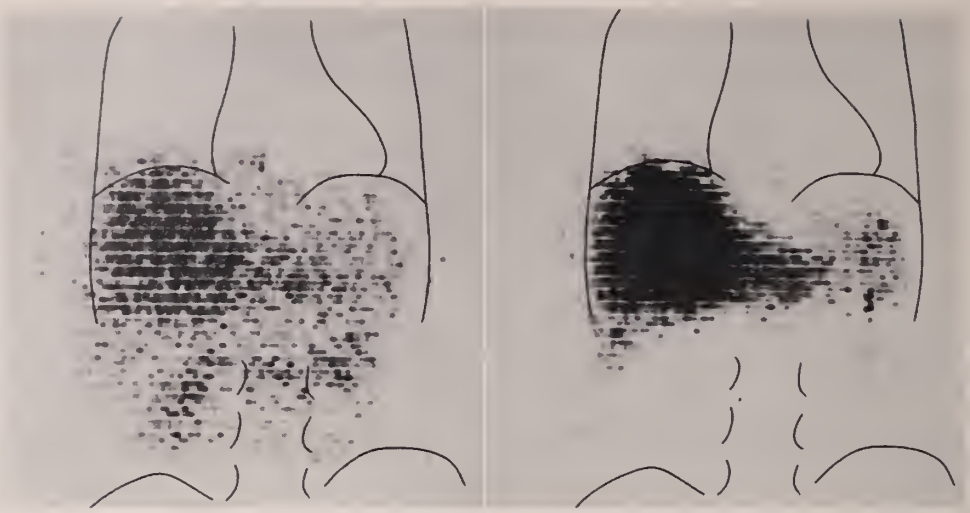


Fig. 2—Normal pancreas (proved surgically), but image is not as dense as in Figure 1. *Left,* Selenomethionine. (From McGill DB, Tauxe WN: Radioisotope scanning of the pancreas. Med Clin North Amer 54:881-888, 1970. By permission of W. B. Saunders Company.) *Right,* ^{131}I-labeled Rose Bengal.

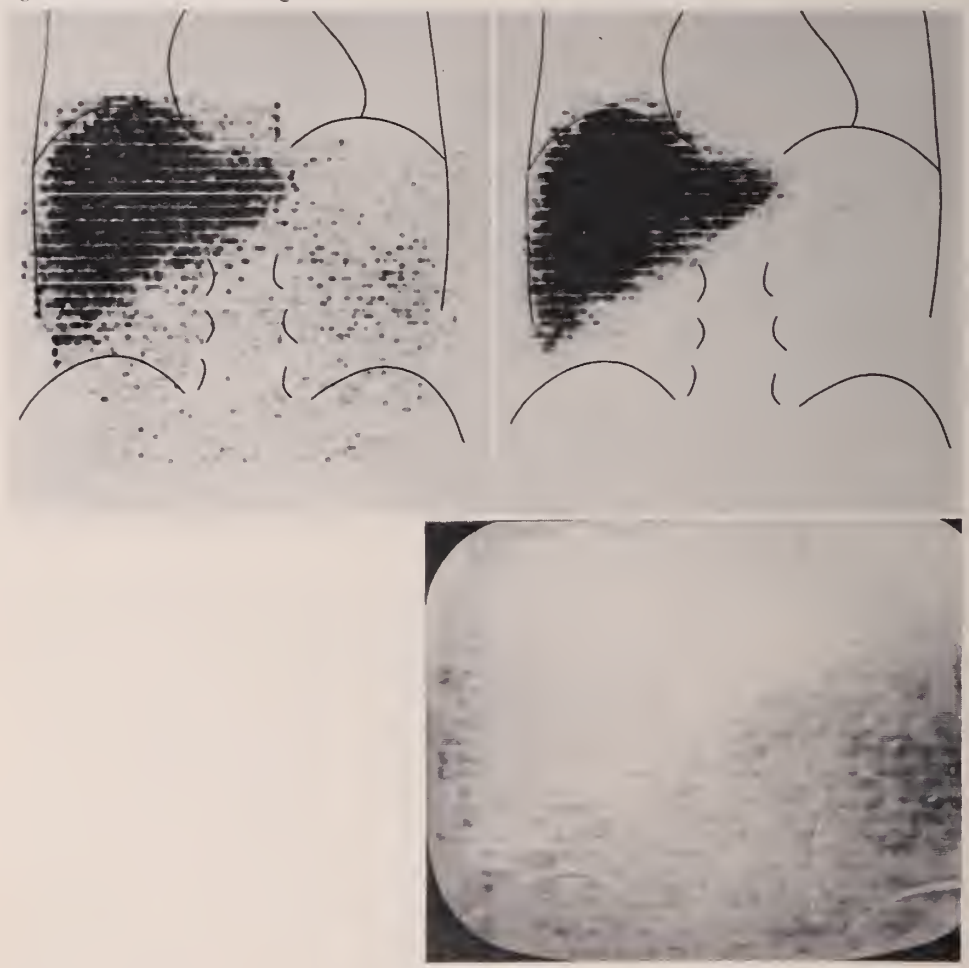


Fig. 3—*Upper,* No pancreatic image can be detected visually. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal. *Lower,* Subtraction scan shows no pancreatic uptake, and operation demonstrated carcinoma. (From McGill DB, Tauxe WN: Radioisotope scanning of the pancreas. Med Clin North Amer 54:881-888, 1970. By permission of W. B. Saunders Company.)

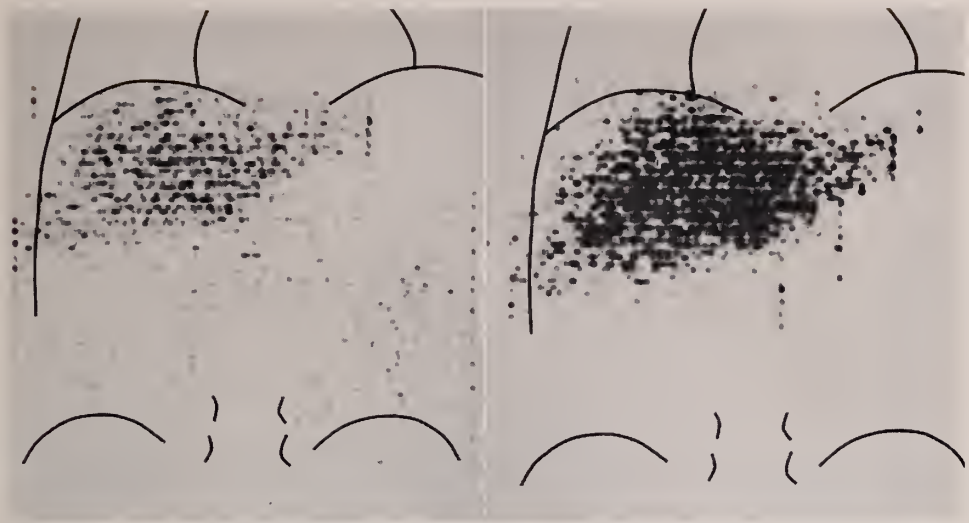


Fig. 4—No pancreatic image can be recognized visually. However, this pancreas proved to be normal. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal.

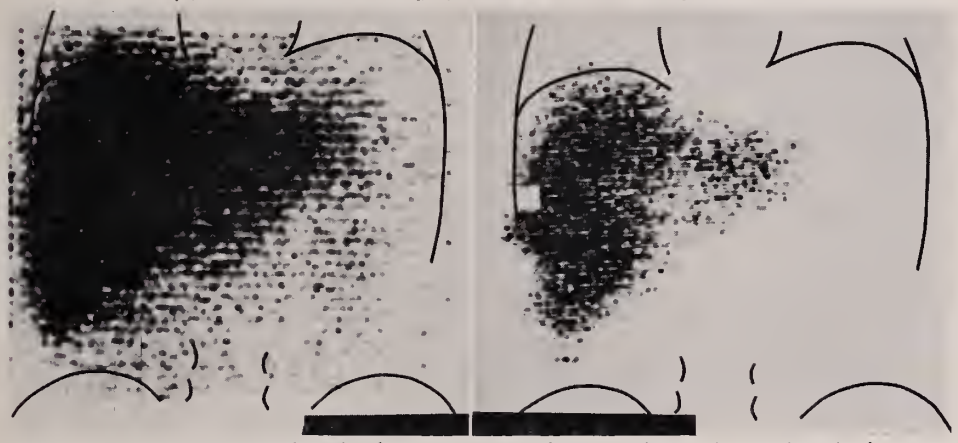


Fig. 5—Three observers found this scan to be uninterpretable and two thought it normal. Operation revealed large carcinoma in head of gland. In retrospect, perhaps the evidence is here but the element of guesswork is obvious. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal.

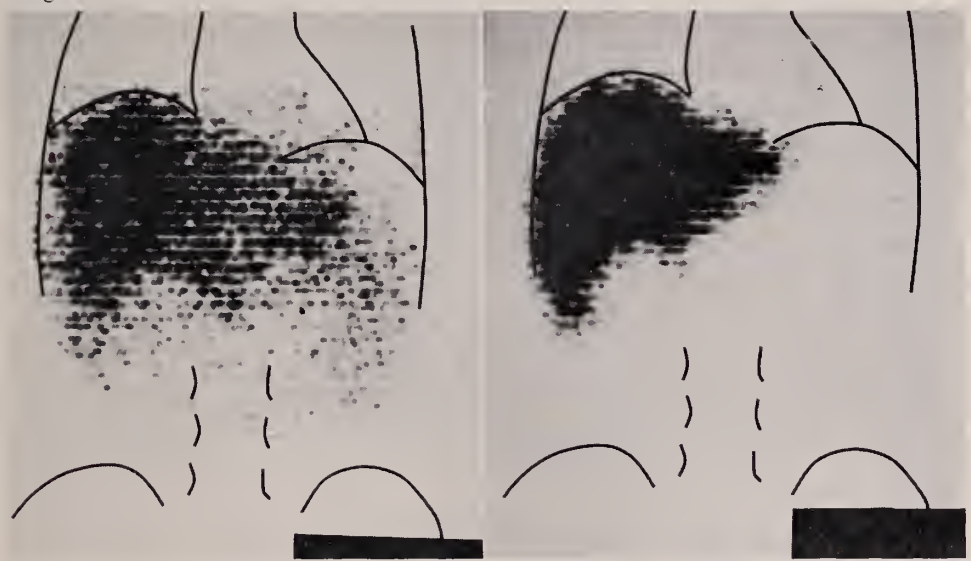


Fig. 6—One might imagine abnormalities in image, as three of five observers did in this review, but pancreas proved to be normal at operation. Subtraction scan (not shown) was similarly misleading. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal.

At present we are at an impasse, awaiting the development of material which will be taken up selectively by pancreatic tissue or of techniques to define the normal gland better. Extrapancreatic uptake, failure of the normal pancreas to visualize, and apparent decrease in uptake with resulting vague filling defects contribute to frequent false-positive scans. Subtraction techniques often eliminate the problem of the overlying liver, but our data to date suggest that electronic subtraction only occasionally offers greater benefit than visual subtraction. Computer analysis and scinticamera techniques, currently undergoing evaluation, should be substantial improvements.

A test which offers a potential accuracy of 6[illegible] to 90% on attempted readings in difficult clinical situations may be of some value if the test can be performed with little or no risk and at minimal cost. The radiation risk of a pancreatic scan is probably negligible, and the expense can be decreased. Occasional scans will reveal classic findings (Figure 8) which should help the clinician. The success of these scans tends to be buried in our overall meager results.

See page 804 for References 1-16.



Fig. 7—Extrapancreatic uptake and adjacent liver make pancreatic image difficult to outline. This 67-year-old woman was recovering from mild pancreatitis. One should probably record this image as normal or indeterminate and wonder about possibility of filling defect in body. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal.

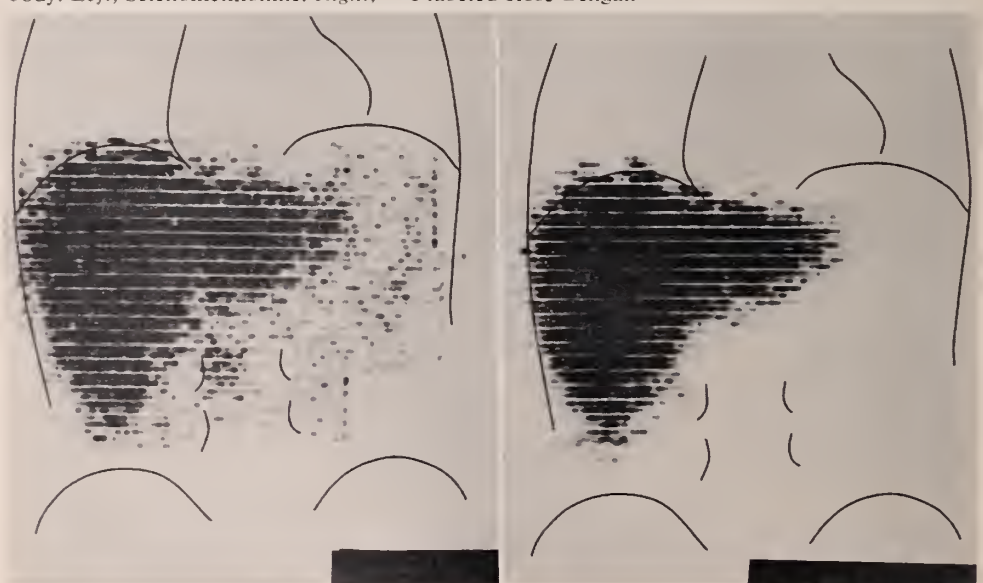


Fig. 8—This and scans in Figures 1 and 2 justify further efforts to refine technique. Head of pancreas is evident but body and tail are cold. At operation, carcinoma involving predicted areas was found. *Left,* Selenomethionine. *Right,* ^{131}I-labeled Rose Bengal. (From McGill DB, Tauxe WN: Radioisotope scanning of the pancreas. Med Clin North Am 54:881-888, 1970. By permission of W. B. Saunders Company.)

Adreno-Cortical Adenoma With Malignant Hypertension

Report of One Case

RAFAEL CARMENA, M.D. AND JOHN I. COE, M.D.

THE HYPERTENSION SEEN in patients with primary aldosteronism is usually of moderate severity.[1] Only a few cases of well documented primary aldosteronism associated with malignant hypertension have been reported.[2-5] We have studied a patient with malignant hypertension who had normal aldosterone values in urine and normal-appearing adrenal glands at exploratory laparotomy. He died after a nine-year course of what was considered to be essential malignant hypertension. At autopsy a cortical adenoma measuring 1 cm. in diameter was found in the right adrenal gland. Evidence is presented which suggests that this may have been a primary aldosteronoma.

Case Report

A 30-year-old man was found to have hypertension in 1960 in a pre-employment examination. He was asymptomatic until 1962 when he consulted a physician because of nervousness and headaches. He was again found to have an elevated blood pressure, and was treated with antihypertensive medications. No family history was available since the patient was adopted. At 35 years of age he was admitted to another hospital complaining of shortness of breath on exertion and ankle edema. The physical examination revealed a slender Caucasian individual with a blood pressure of 196/150. The fundoscopic examination showed a grade II Keith Wagner hypertensive retinopathy. The pulses were equal in all extremities. Auscultation of the heart revealed a regular rhythm and no murmurs. The point of maximal impulse was at the fifth intercostal space in the anterior axillary line. There were bilateral pulmonary basilar rales. The liver was felt four cm. below the right costal margin. No bruit was heard over the abdomen. The lower extremities had 3+ pitting edema.

The laboratory studies included normal complete blood counts; serum sodium, 142 mEq/L, potassium four mEq/L, chlorides 96 mEq/L, and carbon dioxide content 34 mEq/L. The urine gave a 3+ test for albumin and contained small numbers of red blood cells. The fasting blood glucose was 92 mg%. The blood urea nitrogen was 30 mg% but subsequently fell to 19 mg%; the serum creatinine 1.9 mg% and the creatinine clearance 115 ml/min. An electrocardiogram showed first degree atrioventricular block, left axis deviation and left ventricular hypertrophy. The chest Xray showed globular enlargement of the heart with moderate pulmonary edema. Intravenous pyelogram and radioisotope renogram demonstrated bilaterally reduced renal function. A renal arteriogram suggested a deformity of the left renal artery and a selective left renal arteriogram showed a "somewhat small" superior left renal artery with possible stenosis. A 24-hour urine collection showed normal VMA and aldosterone values; no renin studies were done. Because of the possibility of renal artery stenosis an exploratory laparotomy was performed. There was no pressure gradient between the left renal artery and the aorta. Both adrenal glands were palpated and thought to be normal. The patient was diagnosed as having essential hypertension and was discharged on digitalis, reserpine, guanethidine and hydrochlorothiazide.

During the next four years he was followed at the outpatient clinic in Hennepin County General Hospital, and his blood pressure fluctuated between 130/80 and 210/130. He was able to work only five hours per day as he tired easily and had frequent headaches. He developed severe hypertensive retinopathy, including papilledema. His medications included digitalis, hydralazine, methyl-dopa, guanethidine, K-triplex and intermittent thiazides. He complained of persistent leg cramps which seemed to be exacerbated by thiazide diuretics and relieved to some extent by the administration of potassium salts. He complained also of nocturia (urine volume three times greater during the night than day) and was constantly thirsty. He was free of edema during this time. His urine had a pH of eight, specific gravity 1.021 and contained 1+ protein. The creatinine clearance was 150 ml/min. and the blood urea nitrogen 22 mg%. Determinations of serum electrolytes found the sodium ranging from 143 to 148 mEq/L, potassium from 2.4 to 4.3 mEq/L, chlorides from 93 to 105 mEq/L and the carbon dioxide content from 28 to 38 mEq/L. Urinary electrolytes, with the patient on a 2 Gm. salt diet and off thiazides, were sodium 55 mEq/L and potassium 81 mEq/L. His plasma volume (determined with radioiodinated serum albumin) was 3850 ml, +114% of the predicted value.

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In March 1969, the serum sodium was 145 mEq/L, potassium 2.6 mEq/L, chlorides 95 mEq/L, carbon dioxide content 38 mEq/L and the blood pressure 190/110. The patient had been off thiazide diuretics for several weeks. All medications but digitalis were discontinued and he was started on 6 Gm. sodium chloride and 600 mg. of Spironolactone per day. Seven days later the serum sodium was 142 mEq/L, potassium 3.6 mEq/L, chlorides 103 mEq/L and carbon dioxide content 26 mEq/L. Two weeks later the blood pressure was stable about 150/80. There was no evidence of heart failure. The possibility of the patient's having primary aldosteronism was considered in spite of his previously negative workup. He was admitted for another study. On the second hospital day the patient developed severe pulmonary edema, intractable heart failure and expired in cardiogenic shock.

Autopsy

Postmortem examination revealed severe heart disease, congestive failure, and an adrenal cortical adenoma on the left with mild cortical atrophy of the right adrenal.

The heart weighed 900 grams showing marked left ventricular hypertrophy consistent with hypertensive cardiomegaly. Valves were normal. The coronary arteries revealed moderate sclerosis and there was extensive myocardial fibrosis with an area in the anterolateral wall of the left ventricle representing a healed subendocardial infarct.

The liver and spleen showed passive congestion, while the lungs were heavy and edematous. The left and right kidneys weighed 190 and 170 grams respectively. Their surfaces were mottled and pitted.

The left adrenal gland contained a sharply circumscribed bright yellow adenoma 1.2 cm. in diameter distending the medullary portion of the gland. The right adrenal was smaller than normal with the cortex thin and atrophic.

Sections of the adrenal cortical adenoma showed a circumscribed tumor appearing to arise from the zona reticularis which was composed of large clear cells in which the nuclei varied in size with a few large dark nuclei being evident (Figure 1). No mitotic activity was seen. Portions of the adenoma fixed in Zenker's solution showed no dichromate reduction.

The right adrenal showed mild thinning of the



Fig. 1—Adrenal cortical adenoma (X40). The cells of the adenoma were large with clear cytoplasm and varying sized dark nuclei.

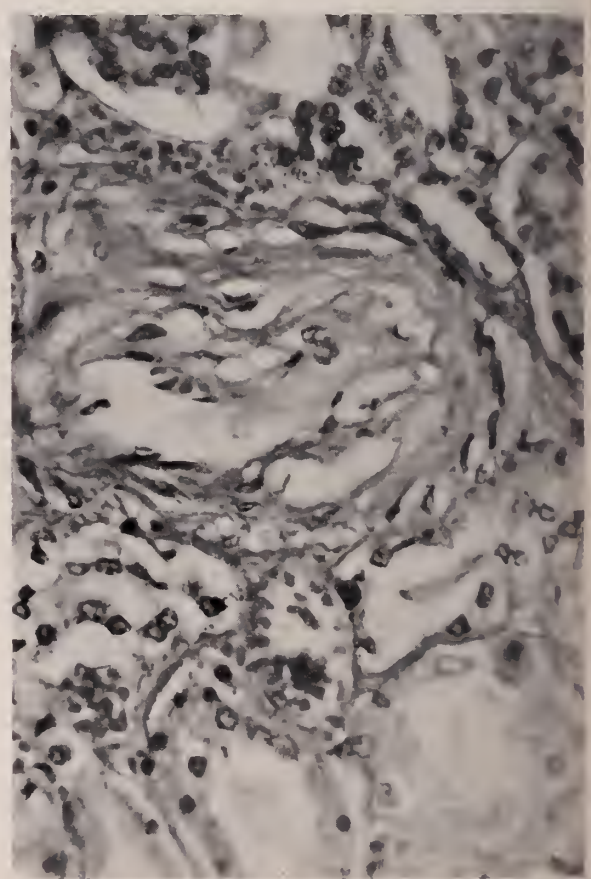


Fig. 2—Renal arteriole (X415). There is endothelial proliferation, splitting of fibers and edema of the vessel wall.

cortex due to atrophy of the zona glomerulosa but was otherwise histologically normal.

The kidneys revealed congested but essentially normal glomeruli and tubules. Large blood vessels revealed only mild medial sclerosis. In contrast small muscular arteries and arterioles all showed medial and intimal proliferation. This was most apparent in the intima where splitting of fibers and edema greatly narrowed the lumina (Figure 2). Many arterioles revealed occlusive intimal proliferation although no fibrinoid degeneration of vessel walls was noted. The histology was felt to be consistent with that found in malignant hypertension.

Discussion

The case presented is that of a 39-year-old man with malignant hypertension and an adreno-cortical adenoma of the right adrenal gland. A study of the patient's hypertension done at another hospital in 1964 was non-revealing, including laboratory studies of the serum electrolytes, urine studies for aldosterone and vanyl-mandelic-acid, and abdominal angiography. A laparotomy disclosed normal renal arteries and adrenal glands.

It is surmised that the adrenal tumor found at autopsy was active as evidenced by atrophy of the zona glomerulosa in the contralateral adrenal cortex. This finding has been reported by others and presented as evidence of functionally active adrenal tumor.[6]

He had a persistent hypernatremia and hypokalemic alkalosis that was accompanied by severe muscle weakness even when thiazide diuretics were discontinued. The patient had responded to the administration of spironolactone with correction of the electrolyte imbalance and significant fall of the blood pressure to normal diastolic values. It has been suggested[7-9] that this type of response is characteristic of primary aldosteronism.

The patient complained of nocturia and polydipsia while maintaining adequate renal function. He had minimal or no edema for the last four years of his life. The hypernatremia, hypokalemia, hypochloremia and elevated plasma carbon dioxide content became normal by the administration of spironolactone, with a decrease to normal of the diastolic blood pressure. These data suggest that the adrenal tumor may have been a primary aldosteronoma.[9]

Sutherland et al.[10] have described two patients with benign hypertension, potassium depletion, increased aldosterone secretion, raised plasma volume, suppressed plasma renin activity and intermittent elevation of 17-ketosteroids and 17 hydroxicorticoids in the urine. These abnormalities disappeared when the patients were given dexamethasone. In one of the patients, large doses of spironolactone corrected the electrolyte imbalance and brought the blood pressure to normal levels. This patient had the adrenal glands explored and multiple, small nodules (0.1-0.4 cm. in diameter) were found in one of the glands. Patients with primary aldosteronism do not respond to the administration of dexamethasone and usually have normal urinary 17-KS and 17-OHCS. The possibility of our patient having a condition similar to the one described by Sutherland cannot be totally excluded.

The question arises whether the patient had malignant hypertension associated with secondary aldosteronism or whether the adreno-cortical adenoma had produced primary aldosteronism with malignant hypertension.

Malignant hypertension is almost universally associated with secondary aldosteronism.[11] Characteristically, one finds low or normal serum sodium levels, hypokalemia and elevated plasma bicarbonate content. A normal or elevated serum sodium, as found in our patient, is rare in essential hypertension.[12,13] The patient had an elevation of his plasma volume of +114% of his predicted value. Increases in plasma volume have been reported in patients with primary aldosteronism, while patients with essential hypertension or renal arterial lesions characteristically have normal to decreased plasma volumes.[13]

The administration of spironolactone to patients with secondary aldosteronism will correct the electrolyte imbalance but has little or no effect on the blood pressure levels.[9] In our patient, as in other patients with primary aldosteronism, administration of spironolactone corrected the electrolyte abnormalities and produced a significant drop in the blood pressure. Secondary aldosteronism is associated with bilateral adrenal hyperplasia, but not a unilateral adenoma. It is possible that the subject studied had a functioning adenoma of the right adrenal gland cortex with a clinical picture of primary aldosteronism.

The patient had a single determination of urine aldosterone that was reported normal. This fact does not necessarily exclude a functioning aldo-

steronoma since plasma and urine aldosterone concentrations may vary considerably in patients with primary aldosteronism.[14]

Until recently, the occurrence of malignant hypertension in patients with primary aldosteronism was considered extremely rare.[1] In 1963, Kaplan[2] reported the first patient with malignant hypertension with clinical and laboratory features of primary aldosteronism.

Brown et al.[3] described a case of adreno-cortical adenoma with hypertension and arteriolar fibrinoid lesions found at renal biopsy. del Greco et al.[4] reported a case of primary aldosteronism with malignant hypertension. The patient had papilledema, exudates and hemorrhage in the optic fundi. Microscopic examination of the kidneys showed mild arteriolar nephrosclerosis. Our case had an adreno-cortical adenoma and severe hypertension, with Grade V retinopathy and proliferative arteriolitis in the kidneys. Smithwick et al.[15] reported two patients who had a negative bilateral adrenal gland exploration because of hypertension and clinical aldosteronism and were later discovered to have a functioning, isolated cortical adenoma measuring two and 1.8 cm. in diameter respectively.

The case presented should serve as a reminder that a primary aldosterone-secreting tumor may precipitate malignant hypertension and one should consider such possibility when dealing with patients with both the benign and malignant type of hypertension. A single determination of urine aldosterone and a negative surgical exploration of the adrenal glands do not exclude the presence of a functioning adreno-cortical adenoma. Repeated urine aldosterone and plasma renin determinations might have been helpful.

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Spontaneous Subarachnoid Hemorrhage

Initial Presentation of Brain Tumors

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SUBARACHNOID HEMORRHAGE has many causes. This is well illustrated by Walton,[12] who in an excellent review article listed over 40 possible conditions which may produce subarachnoid hemorrhage. Despite this fact, in many physicians' minds subarachnoid hemorrhage is almost exclusively related to ruptured intracranial aneurysms. This is not without some justification, since the "Report on the cooperative study of intracranial aneurysms and acute subarachnoid hemorrhage"[7] found that 51% of subarachnoid hemorrhages are due to ruptured aneurysms. A significant percentage remains, however, due to other etiologies. Brain tumors are one such relatively unusual source of subarachnoid hemorrhage. This paper concerns the clinical problem of brain tumors presenting with subarachnoid hemorrhage.

In 1924, Symonds wrote the first systematic review of spontaneous subarachnoid hemorrhage.[11] He discussed tumors and cysts as a possible source of subarachnoid hemorrhage and presented two such cases. Over the next several years there were several published case reports of brain tumors presenting with subarachnoid hemorrhage; sometimes repeated and diffuse.[3,4,5,10]

In 1955, Glass and Abbott[6] reviewed the literature and found 41 cases of brain tumor presenting with the abrupt onset of subarachnoid hemorrhage, mimicking aneurysm. They added seven additional cases of their own. The exact number of hemorrhages could not be determined in all instances; but of 36 patients all but six had more than one hemorrhage. Of the 41 cases analyzed, 50% of the tumors were primary gliomas of the cerebrum with 12 of the 20 being malignant astrocytomas. Pituitary lesions, mainly adenomas, accounted for the second largest category, with 11 cases. The mechanism of hemorrhage was postulated to be the same as that for intraparenchymal hemorrhage into most malignant gliomas, i.e. vascular endothelial proliferation with resultant vessel occlusion, secondary necrosis and loss of vessel support, leading to hemorrhage. Signs and symptoms were those typical of subarachnoid hemorrhage of any cause, namely headache, nausea and/or vomiting, nuchal rigidity and altered consciousness.

The following case history emphasizes the diagnostic difficulties encountered when this situation presents.

Case Report

This 44-year-old man was admitted to the Minneapolis Veterans Administration Hospital on January 9, 1967, with a history of the sudden onset of severe left sided headache on January 3, 1967. This was accompanied by photophobia, nuchal rigidity, rather marked mental confusion, and disorientation. Historically the patient had had an identical episode about one month previously. These symptoms subsided spontaneously over a few hours, with the exception of mild personality change and a minimal degree of alexia. The patient sought no medical attention until after the second episode.

Examination

The patient was slightly confused and disorientated and had an obvious expressive and receptive aphasia. There was some degree of nuchal rigidity, but otherwise the general physical and neurological examinations were completely normal. A lumbar puncture demonstrated grossly bloody spinal fluid.

The initial impression of the examining surgeons was that of subarachnoid hemorrhage, likely secondary to an intracranial aneurysm along with a probable left temporal lobe hematoma. On January 10, 1967, bilateral carotid angiography revealed a large avascular lesion within the left temporal lobe. There was no demonstrable aneurysm, nor was there any evidence of vasospasm of the intracranial vessels. Similarily there was no evidence of "tumor stain."

Surgery

The following morning the patient was taken to the operating room where upon opening the dura the expected subarachnoid hemorrhage was noted. Additionally, much as anticipated, a rather large hematoma was encountered within the left temporal lobe. Following

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See editorial, page 819.

evacuation of the hematoma, abnormal appearing tissue was encountered in the depths of the hematoma cavity. This was biopsied and frozen section confirmed the presence of malignant glial tumor. A modified temporal lobectomy was carried out.

Postoperative Course

Postoperatively the patient's prior aphasia and alexia cleared nearly totally. Permanent pathological specimens confirmed the tumor to be a glioblastoma multiform. The patient received a course of radiation therapy in the postoperative period and did reasonably well for eleven months. He then deteriorated, expiring on January 31, 1968.

Discussion

The "Report on the cooperative study of intracranial aneurysms and acute subarachnoid hemorrhage"[7] found the incidence of subarachnoid hemorrhage associated with brain tumors to be about two percent. However, if one limits the criteria to those in which the clinical onset is abrupt and thereby closely mimics subarachnoid hemorrhage for aneurysm, it is a relatively unusual event.

This case of a previously asymptomatic man with two typical attacks of subarachnoid hemorrhage emphasizes that subarachnoid hemorrhage is not an entity in itself. Although aneurysm is its most common cause, various other pathological processes must be considered, especially when angiography does not reveal an aneurysm, vascular malformation, or other obvious source for the hemorrhage. Under these circumstances a complete evaluation and thorough appraisal of the problem is indicated, since even benign lesions, such as meningiomas and pituitary adenomas have occasionally presented with typical signs of subarachnoid hemorrhage.[1,2,8,9]

Summary

We have reported a case of a previously asymptomatic man who presented with a picture typical of repeated acute subarachnoid hemorrhage. The presumed diagnosis was that of a ruptured aneurysm or cryptic vascular malformation, until the time of surgery, when in addition to the findings of a typical subarachnoid hemorrhage, a large malignant glial tumor of the left temporal lobe was then identified. This case emphasizes that aneurysms and vascular malformations are not the sole cause of acute subarachnoid hemorrhage or even repeated episodes of subarachnoid hemorrhage. Other possible etiologies must be especially sought when angiography fails to reveal an obvious source of hemorrhage.

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Intravenous Lidocaine for Status Epilepticus

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THE DRUG OF CHOICE today for status epilepticus is probably intravenous diazepam.[1] It is effective and relatively nonsedating (in comparison to the barbiturates). Some clinicians prefer intravenous, rapidly acting barbiturates, or Dilantin. Paraldehyde is occasionally recommended. If all else fails, general anesthesia is recommended as a "last resort."

This is a report of the use of another anesthetic drug, intravenous lidocaine. Indications for the use of lidocaine are not limited to producing conduction block anesthesia. Bernhard,[2] following several reports of the effectiveness of local anesthetics in animals,[3] first reported the use of intravenous lidocaine in the treatment of humans with status epilepticus. This treatment with lidocaine has been documented in the medical literature and reference books.[4,5] The use of lidocaine is, however, not well known and most "emergency" manuals fail to mention lidocaine as a possible therapeutic agent.[6,7]

Case Report

The patient was a 45-year-old, 213 lb., white male who was admitted to hospital because of recurrent and frequent seizures. In 1944, the patient was in an auto accident in which he sustained a severe head injury and was unconscious for several days. Subsequently he had had recurrent major, minor and right-sided Jacksonian seizures. He was a chronic alcoholic and was said to have "Chronic Brain Syndrome." His anticonvulsant medication consisted of taking Dilantin (100 mg. t.i.d.) and phenobarbital (60 mg. t.i.d.) which he took regularly. He had had previous episodes of status which numbered about 10 and had always been promptly relieved by intravenous barbiturates (in recent years by intravenous diazepam). There was no recent history of infection or other drug ingestion, except for small doses (25 mg. t.i.d.) of Mellaril. He said (later) that he had been seizure free for about four years.

Recently he had been admitted to another hospital after at least two grand mal seizures and recurring focal Jacksonian seizures every 10 minutes. The physical exam revealed an obese, dazed, mildly dysarthric white male with nystagmus on lateral gaze. No paralysis was noted. Babinski signs were present bilaterally. The patient was treated with intravenous and intramuscular doses of diazepam (10 mg. IV, four times in 12 hours), intravenous Dilantin (500 mg.), phenobarbital (120 mg., IV) and magnesium sulfate (1 gram in each buttock). After two days of frequent seizures uncontrolled by the above medications, he was unimproved and nearly comatose. He was then transferred to the Minneapolis Veterans Hospital.

Physical Findings

After transfer, his vital signs were stable and normal. He was unresponsive and having Jacksonian type seizures that began on the right side of his face and spread to the right side of his body, without becoming generalized. His neck was supple and his eyes deviated conjugately to the right. There was no papilledema. Bleeding from the tongue was noted. He did not move his extremities on command. His reflexes were sluggish and there were no abnormal toe signs. The patient withdrew each extremity to painful stimulation.

Hospital Course

During the next two days the patient continued to have focal seizures every three to four minutes. Occasionally a period of 20 minutes would elapse between seizures, but consciousness was not regained between seizures. Twenty mg. of diazepam IV was given every hour times three. Paraldehyde per rectum (20 ml.), Dilantin (1 gram IV) and large doses of phenobarbital (100 mg. Q4h) were administered. His seizures, however, continued. He was subsequently intubated because of respiratory supression and steroids were given.

Laboratory Data

Routine laboratory work, including spinal puncture was unremarkable. There were 12 RBCs and 59 WBCs in the CSF after three days of status. A left carotid angiogram was normal. An electroencephalogram was done while he was in status and showed hemispheral assymetry with depression of the faster frequencies and amplitude with low voltage spikes and excessive, diffuse, slowing.

After the above measures failed to halt his continuous seizures, general anesthesia was considered. At the suggestion of one of the authors (A.W.K.) intravenous lidocaine was used. The patient was given 150 mg. of lidocaine IV and one gram of lidocaine in 250 cc of

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5% dextrose in water was dripped in over one hour. About five minutes after the IV bolus of lidocaine was given, the patient manifested one mild focal seizure. Following this, he was seizure free. He was subsequently given one more lidocaine drip (one gram in 250 cc of fluid) over the next six hours. The lidocaine was discontinued and the patient was maintained on Dilantin (100 mg. t.i.d.) and phenobarbital (30 mg. t.i.d.). He woke slowly over the next few days and developed pneumonia and asthmatic bronchitis which responded to appropriate treatment.

At the time of discharge from hospital, there were minimal signs of left cortical involvement. The patient was alert and the mental examination was within normal limits. The patient still insisted that he had been taking his medicines faithfully. He also denied an excessive use of alcohol. He said cheerfully when he left: 'I'll see you guys the next time I go into status."

Trade names: Dilantin—diphenylhydantoin sodium. Xylocaine—lidocaine.

Indications and Side Effects

Although intravenous diazepam is the drug of choice for status epilepticus, intravenous lidocaine may also be an effective agent when diazepam fails. Potential disadvantages of lidocaine are: (1) possible allergic reaction; (2) depression of the myocardium; and (3) paradoxically, seizures. (Why the drug should be effective in the control of status epilepticus, yet instigate seizures occasionally has not yet been fully explained).

Administration

We recommend the use of intravenous lidocaine in the following manner. First, as intravenous bolus of 1.5 mg/kg., followed by an IV drip of 10 mg/kg. in D5W run in over four to six hours. The drip may be repeated if necessary. The patient should be continuously monitored with EKG and probably would be best managed in an intensive care unit under the supervision of appropriately trained personnel. Naturally, possible inciting causes for the status such as brain abscess, subdural hematoma or other irritative lesions must be vigorously investigated.

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Cover Painting

"Pleasant Lake"

Doctor Harry B. Clark tells us: "After World War One I settled in St. Cloud, where I was born, and engaged in general practice until about 13 years ago when I became a member of the St. Cloud Veterans Hospital staff, where I still am. I always wanted to paint, but like so many people, didn't believe I possibly could. About 20 years ago I tried copying a picture using one of my children's water color sets just to see what I could do. I liked it well enough and enjoyed doing it so much I just kept on. Later I added oil painting and recently have experimented with acrylics.

The painting itself is a lake near St. Cloud called Pleasant Lake. It is not how it looks today, with permanent homes all around it, but as it looked many years ago when there were only a few summer cottages and one of them mine. Mist must still form on the surface of the lake on chilly mornings, but I doubt if the blue herons still can be seen. That is one of the advantages of painting over photography, you can depict past, present or future and put in characters like blue herons that do not sit for photography."

Thymectomy

In Fulminating Myasthenia Gravis of Childhood

KENNETH F. SWAIMAN, M.D. AND RICHARD L. VARCO, M.D.

Following the neonatal period, the incidence of myasthenia gravis is very low until after five years of age.[1] Although neonatal persistent myasthenia gravis rarely embarrasses the bulbar muscles or muscles of respiration, myasthenia gravis appearing later in the first decade can be a cataclysmic affair.[2] After early years of controversy, punctuated by transatlantic debate, thymectomy has been accepted as a method of therapy which is frequently successful in young women without thymomas, who have had the disease for a short period of time.[2] Recently, it has been suggested that thymectomy has little value in the young child.[3] This is a report of a thymectomy performed on a 28-month-old myasthenic child that was life-saving.

Case Report

This male child was first admitted to the University of Minnesota Hospitals at age 22 months in January 1967 with a four week history of left eyelid ptosis and a one week history of "his eye turning out".

He had been in good health except for a short episode of pneumonia at age seven months. His mother did not have myasthenia and has not subsequently developed the disease. The general physical and neurological examination were normal with the exception of bilateral ptosis and left exotropia. He was given 1.0 mg of edrophonium chloride intravenously with marked improvement of both the ptosis and exotropia.

Thyroid function studies and blood electrolytes were normal. Chest Xray was normal. Electromyography (EMG) revealed no decrease in amplitude of action potentials during repetitive supramaximal stimulation of the ulnar nerve.

Therapy with oral neostigmine chloride was begun at a dose of 10 mg every four hours and increased to 15 mg every four hours. The ptosis and squint were improved and he was discharged on February 2, 1967.

His clinical course is charted in the Table. Briefly, he developed bulbar weakness which progressed rapidly in addition to the weakness of his extraocular muscles despite large doses of anticholinesterase drugs. (He was receiving pyridostigmine 60 mg every four hours and neostigmine 20 mg every two hours. Edrophonium chloride administration increased strength, but increased secretions also.) He had progressive difficulty swallowing and controlling his secretions. Right upper lobe atelectasis appeared. He had several episodes of apnea and bradycardia. In April of 1967, after an abrupt episode of apnea, a tracheostomy was performed. He became severely ill with pneumonitis, respiratory weakness in May of 1967 and became progressively worse. He underwent a thymectomy and gastrostomy on July 19. Microscopic examination of the thymus revealed simple hyperplasia. He had a stormy postoperative course primarily because of profound residual pneumonitis. He improved remarkably after the thymectomy and necessitated only small doses of anticholinesterase drugs to allow him to control his secretions and alleviate his ptosis and squint.

Attempts at removing the tracheostomy tube over the

TABLE
Clinical Course

	Clinical findings	Therapy
Jan/67	Ptosis Exotropia (age 22 months)	
Feb/67	Ptosis Exotropia	Neostigmine-p.o. (10-15 mg/q4h)
March/67	Increased Weakness Extraocular Muscles	Neostigmine-p.o. (20 mg/q4h)
April/67	Acute apnea Pneumonitis	Tracheostomy Neostigmine-p.o. (20 mg/q4h) Pyridostigmine-p.o. (60 mg q4h)
May/67	Bilateral ptosis Poor cough Hyperpnea	Neostigmine-p.o. (30 mg/q2h) Pyridostigmine-p.o. (90 mg/q4h)
June/67	Pneumonitis	Neostigmine-I.M. (0.5 mg/q2h)
July/67	Pneumonitis	Thymectomy Gastrostomy *Neostigmine (10 mg/q2h) *Atropine (0.1 mg/q3h)
Aug/67	Decreased Pneumonitis	*Pyridostigmine-p.o. (60 mg/q3h)
Feb/67	Ptosis Exotropia Swallowing improved Discharged from hospital	*Pyridostigmine (25 mg/q3h) *Atropine (0.1 mg/q3h)

*Through gastrostomy tube.

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was primarily prolonged by difficulty of residential placement. He was discharged on February 2, 1969 on pyridostigmine bromide 25 mg every three hours, and atropine 0.1 mg every three hours which was needed to control nasopharyngeal secretions.

By March 1972, he gradually gained increasing use of his swallowing muscles and he has gained weight and presently attends public school. Supplemental feedings are still administered through his gastrostomy tube although he is able to handle increasingly larger amounts of liquids and solids orally. His tracheostomy was removed in February 1972. He receives pyridostigmine bromide 35 mg every four hours.

Comment

Keynes[2] initially reported that thymectomy was a successful means of managing myasthenia gravis when it appeared in a fulminating form in early childhood.[2] His youngest patient, age two and a half at time of thymectomy, was gravely ill at time of surgery and died postoperatively. Sutin and Hewitson[4] report a 25-month-old child with ocular muscle weakness alone, who responded to thymectomy. Although details are not given, Fonkalsrud and associates reported a two-and-a-half-year-old child who improved after thymectomy.[5] They reported a series of 14 patients, (average age at operation 13.3 years), who underwent thymectomy. Only two patients were under four years of age. Significant improvement occurred in 13 patients.

Myasthenia gravis in children appears in the neonatal period, or towards the middle of the first decade.[1] Onset during the second year is unusual. Furthermore, myasthenia gravis is usually not a rapidly progressive, life-threatening disease when it appears in the middle of the first decade.

We have been impressed with the lack of abnormal electromyographic findings after nerve stimulation in children with myasthenia gravis who do not have peripheral muscle weakness.

During attempts to treat our patient, it became increasingly obvious that he was going to die from aspiration disease despite large doses of anticholinesterase drugs and tracheostomy. Steroid administration was precluded by the presence of severe pneumonia. The profound weakness of oropharyngeal muscles which led to frequent aspiration was controlled after thymectomy with small doses of anticholinesterase drugs. This success contrasted with the massive doses which were ineffectual before thymectomy. The use of a gastrostomy tube facilitated maintenance of adequate nutrition, reduced the likelihood of food aspiration, and allowed safe utilization of oral anticholinesterase drugs.

Summary and Conclusion

Although the source of much speculation, the mechanism by which thymus gland function is related to myasthenia gravis is unknown. Complete remission after thymectomy is unusual. There is no way of confidently determining beforehand, which patients will benefit from thymectomy. This myasthenia patient appears to be one of the youngest subjected to thymectomy who has profited. In any event, this case reaffirms Keynes' initial observations that thymectomy may be life-saving and is beneficial to the occasional patient who has fulminating myasthenia gravis in the first several years of life.[2] In view of this experience and the report of Fonkalsrud and associates,[5] thymectomy for myasthenic children with bulbar weakness or severe limb and trunk weakness, must be seriously considered.

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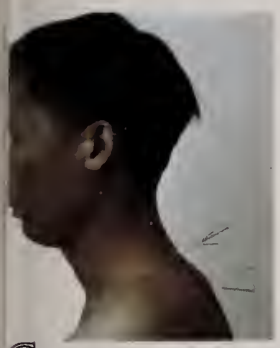
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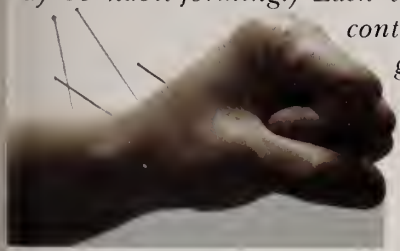
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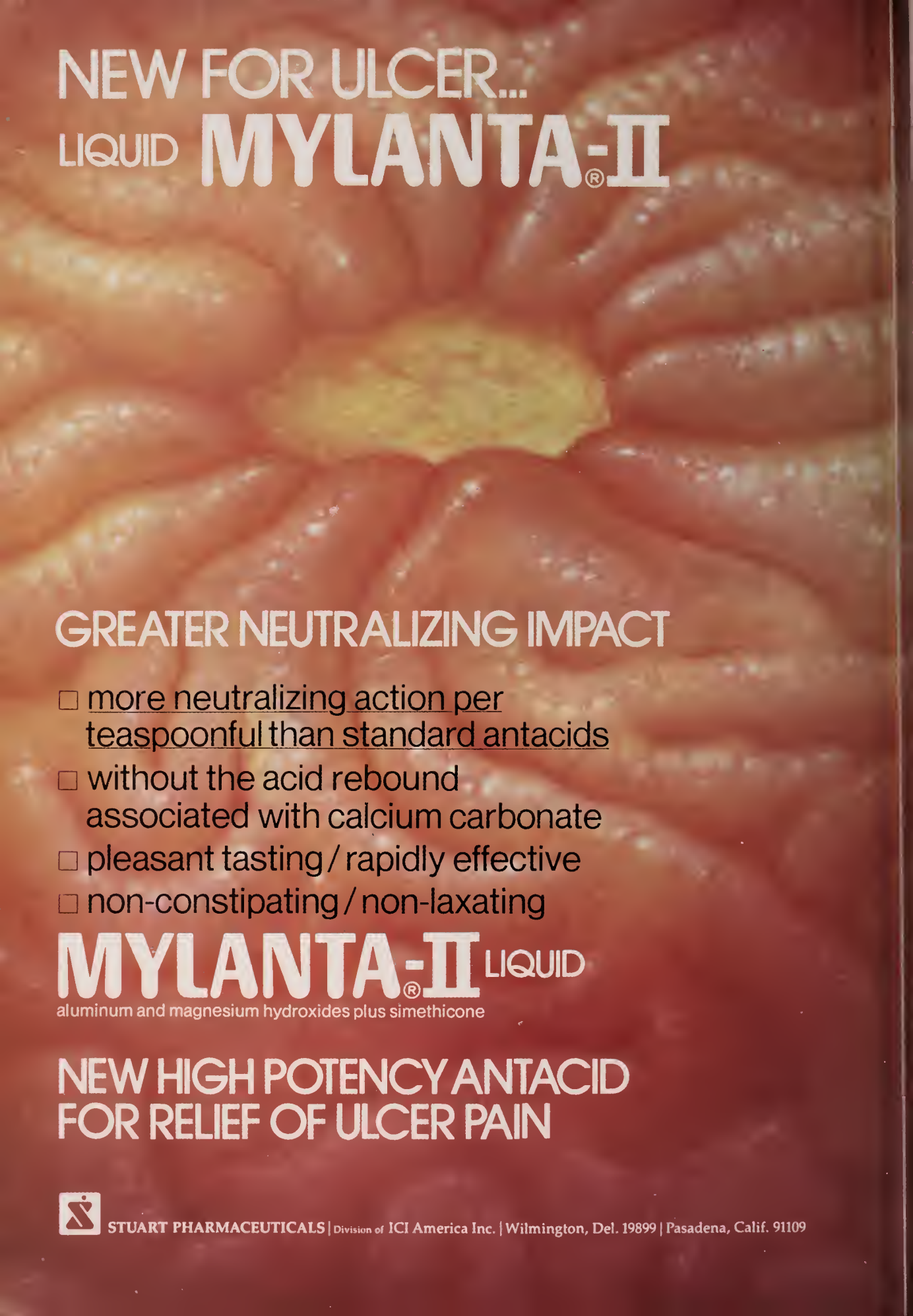
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Editorials

Cancer of the Large Bowel
Problems of Prevalence and Detection

CANCER OF THE LARGE bowel (colon and rectum) takes a formidable toll of life in most countries of western culture. Approximately 45,000 persons die annually of this cancer currently in the United States. The carcinogenic role of soot for chimney-sweep's cancer was pointed out by Percival Pott (1774). Prior thereto, it was believed to be an inherited disease. Prolonged exposure to actinic rays of the sun is recognized as a cause of skin cancer. Polycyclic hydrocarbons and phenolic oils of tobacco are believed to have carcinogenic properties that produce squamous cell cancers amongst tobacco users. The persistence of cigarette smoking, particularly, is generally the acknowledged reason for the great increase in lung cancer over the past three decades. Some investigators incline to the belief that 3.4 benzpyrene is the most active carcinogenic influence in tobacco. Excretion of the carcinogenic substances of tobacco apparently too may have a causative relationship to cancer of the urinary bladder. Aniline dye workers notably are prone to cancer of the bladder.

The genesis of most cancers, however, is obscure. One of the inexplicable and dramatic mysteries of cancer has been a 50% decline in the incidence of gastric cancer in the United States and in many western countries over the past three decades. Could better preservation of food through prevalence of refrigeration be a factor? The benzpyrene generated from frying and roasting of food has long been under suspicion as a causative factor in gastric cancer.

*See page 779.

In the dimsighted groping for a causal relationship of cancer and other diseases, an assessment of geographic distribution is a very natural first resort. Today gastric cancer has its largest mortality rate in two countries widely separated in space and culture, viz., Chile and Japan. The mortality rate of cancer of the large bowel apparently is greatest in Denmark and Scotland. Below the Sahara Desert in South Africa, cancer of the large bowel is apparently rare.

Differences in mortality rates of breast cancer are equally mystifying, relatively uncommon in Japan, the highest rates are found in Holland, England, Denmark and Scotland.[8]

Such geographic studies of cancer incidence stir the imagination, in the absence of causality information, to look for obscure factors of association identified with diet and environmental considerations. Such has been the approach of the eminent investigator of cancer amongst South Africans, Denis Burkitt,* who has boldly suggested in a number of publications (1969-71) that diet, constipation, appendicitis, diverticulitis, and cancer incidence may have similar and related associations.

Every hypothesis or premise needs to be tested. Obstruction in the proximal portion of the vermiform appendix by a fecalith is the causative factor in the genesis of appendicitis. In the presence of obstruction the appendix ruptures because of the singular great secretory capacity of the appendix in the rabbit,[9] chimpanzee[11] and man[10]—exceeding diastolic blood pressure, as studies at Minnesota demonstrated more than three decades ago.

The appendicolith is undoubtedly dietary in origin, but what element in the diet occasions its development remains an enigma. Aschoff[1] (1930) erroneously concluded that the fecalith had no causative relationship to appendicitis because the perforation occurred distal to the obstruction. His inference obviously was that the appendix, attached to the cecum, was poised in favor of absorption rather than secretion. He failed obviously to test his hypothesis.

The evolution of cancer from adenomatous polyps can be traced in the stomach, colon, and rectum. Cancer *in situ* with a long asymptomatic interval is the usual circumstance. Minnesota cancer detection studies suggest that removal of asymptomatic adenomatous polyps in the rectum decreased significantly the anticipated occurrence and incidence of rectal cancer.[2,3]

The most telling observation of 20th century cancer investigators has been that of George Papanicolaou[6] who demonstrated that recognition and destruction of *in situ* cancers of the uterine cervix has reduced the mortality from that disorder in the United States by approximately 60 percent! If all women accepted an annual "Pap smear" and submitted to treatment for a positive finding, mortality from cancer of the cervix could approach the vanishing point.

Today's surgeon of the alimentary tract has access to far more precise and reliable techniques by which to recognize gastric and colic cancers than did surgeons of my generation. Oh, to be a young surgeon again and to have the advantage of current precision techniques for detection of cancers of the gastrointestinal tract! Japanese roentgenographers[5] observed that use of air contrast media enabled them to detect quite regularly mucosal gastric defects whose existence can be confirmed by gastroscopy. Similarly, the Swedish radiographer, Welin,[13] since 1955 has continued to emphasize that adenomatous polyps 5 mm in diameter can invariably be recognized by use of air contrast studies. Unfortunately, neither in Sweden nor elsewhere, where cancer of the colon is frequent, have Welin's findings and advices had the same telling effect on cancer mortality as have the studies of Papanicolaou.

Physicians do have a moral and professional responsibility to respond to significant findings that point the way to improved achievement. Until the causative origins of adenomatous polyps in stomach, colon, and rectum are known, and reliable, preventative measures are devised to preclude their occurrence, what method other than early detection is there to assure continued betterment of the present modest accomplishment?

During the 1920-1940 years, before acceptance of proctocolectomy as the surgical treatment of ulcerative colitis, ileostomy was the standard procedure, when surgery was invoked. Despite deviation of the fecal stream, cancer frequently developed in the remaining large bowel. Similarly surgeons who perfomed colectomy and ileostomy, leaving the rectum, learned that the disease persisted in the residual rectum. There are undoubtedly a large number of patients, some of whose case histories may already have been recorded in the medical literature, who underwent colostomy because of diverticulitis. Did cancer of the rectum subsequently develop amongst any of these patients? Pursuit of such an inquiry could constitute a beginning in testing Burkitt's hypothesis.

During the last quarter of the 19th century, clues for the origin of many infectious diseases were sought in geographic studies. When Fehleisen[4] (1882) discovered and described streptococcus pyogenes, the cause of puerperal fever, erysipelas, and scarlet fever, it was obvious that the geographic incidence studies had no significance.

An annual physical examination, including digital and proctosigmoidscopic examination, as the Minnesota Cancer Detection Center study-experience demonstrates, will detect the presence of adenomatous polyps, some of which on removal are found to harbor *in situ* carcinoma. Hope for a means of nonsurgical removal of some adenomatous polyps in the colon has been quickened by arrival of the flexible colonoscope, also developed by Japanese clinicians, an instrument that already is having wide clinical trials in this country.

Long term followup studies indicate that patients who underwent subtotal excision of the large bowel for cancer, may develop a new cancer in the remaining colic segment a decade and more after the primary near-total colectomy, suggesting that residual colic mucosa, in patients who once had a colon malignancy, still harbors the threat of a new lesion. Such occurrences denote the importance of prolonged followup in all patients submitted to any operative procedure less than total colectomy; and for them an annual visual inspection of the mucosa of the remaining rectum is in order.

While we inch forward year by year in quest of echniques and methods by which the cancer nenace can be overcome, available reliable meth-)ds by which the presence of adenomatous polyps :an be detected, probably the most frequent)recursor of cancer in the large bowel, must not be neglected.

While additional testimony is sought to support the Burkitt hypothesis, that constipation is at the root of the problem of cancer of the large bowel, this observer prefers to align himself with those who ask, what is the factual evidence?

Owen H. Wangensteen, M.D.
Minneapolis, Minnesota

From the Department of Surgery, University of Minnesota, Minneapolis, Minnesota.

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Tetanus

In the United States tetanus is a relatively minor cause of death, compared to heart disease, stroke, cancer, and many other diseases. Despite this, no unimmunized individual is totally safe from this painful and potentially fatal disease. There is no "herd immunity" to protect the person who neglects securing this health protection. Conversely, everyone runs repeated risk of injury which breaks the skin and allows tetanus spores to enter the body.

Once they enter a suitable wound, which may be as tiny as a thorn prick, the dormant tetanus spores revert to their original bacillus form and may begin to multiply. In the process, they liberate a deadly toxin which attacks the central nervous system. Often the first nerves affected are those of the head and neck which control the chewing muscles; these muscles contract rigidly, producing lockjaw.

Despite therapeutic innovations, a patient with tetanus today has about the same probability of dying as he did in 1950, over twenty years ago. That there has been a gradual decline in this period in the numbers of cases and numbers of deaths is a reflection of gradually expanding coverage of the total population with adequate active immunization. Tetanus is a disease of the unimmunized, concentrating on the extremes of age.

Tetanus toxoid is an almost ideal immunizing agent providing effective, long lasting protection. Hypersensitivity reactions may occur in persons who have received an excessive number of booster injections. Toxoid is available in both fluid and adsorbed forms. Comparative tests have shown that adsorbed toxoids are clearly superior in inducing high antitoxin titers. The promptness of antibody responses to booster doses of either fluid or adsorbed toxoid is not sufficiently different to be of clinical importance. Therefore, adsorbed toxoid is the agent of choice for both primary and booster immunization.

Primary immunization of adults consists of a series of three injections, with the second dose four to six weeks after the first, and the third dose six months to one year after the second. Four injections are usually given to children for primary immunization.

Dr. Mark Dahl* is to be commended for reminding physicians of the recent Minnesota experience with tetanus. It should reinforce the urgency of seeing that everyone in the population, including doctors and their wives, receive the protection of tetanus immunization.

D. S. Fleming, M.D.
Minneapolis, Minnesota

*See page 787.

Dr. Fleming is the Director Division of Disease Prevention and Control, Department of Health, Minneapolis.



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Iodine and the Thyroid Gland

DISEASES OF THE THYROID gland occur with considerable frequency in ordinary clinical experience. These conditions occur not only as clinical entities such as myxedema or myxedema coma, but also as complications of other diseases, as exemplified by hyperthyroidism complicating heart failure.

Iodine is fundamental to the functioning of the thyroid hormone. Its curious role in this function is not yet entirely explained. However, a great deal of fundamental information is now made available to us.

The average North American diet contains 100-200 micrograms of iodine daily. It is taken up mostly by the thyroid or excreted by the kidney, and excreted in smaller amounts by the salivary and mammary glands. Iodine is converted in the thyroid gland to triiodothyronine(T3) and to thyroxine(T4), peptides linked in thyroglobulin. The thyroglobulin is stored in the thyroid gland lasting from two to four weeks. Hormones of other endocrine glands are stored in only about a four-hour supply.

Thyroglobulin does not enter the circulation normally. Proteolysis release T3 and T4 from the thyroid gland into the circulation.

Normally 10 micrograms of T4 and 50 micrograms of T3 are secreted into the circulation daily. T4 is bound to proteins which transport it. About one-half of the thyroxine is used up in seven days but one-half of the T3 is used up in a day and a half.

Some measurements of thyroid function depend on determining the quantities of T3 and T4 in the blood.

Wahner's* excellent discussion of the iodine metabolism in the thyroid function in the July issue reviews the important advances in this area. A careful reading of this paper will be helpful to physicians who diagnose and treat thyroid diseases.

Albert J. Greenberg, M.D.
Minneapolis, Minnesota

*Page 623, July, 1972 issue of MINNESOTA MEDICINE.

Cerebral Vascular Accident

THE ARTICLE by Drs. Rockswold and Seljeskog* presents an opportunity to discuss the cerebral vascular accident (CVA). The term CVA refers to the sudden onset of neurologic symptoms in a previously well person and does not indicate a specific pathologic condition. Some have said that the term CVA might well be replaced by the word "stroke." Subarachnoid hemorrhage is one form of stroke and, as the authors point out, can have many causes. In the 45 years since Moniz first described the clinical use of cerebral angiography, marvelous progress has been made, both in the early diagnosis of brain tumors and in our understanding of the pathogenesis of stroke in all its forms.

The use of the term CVA in a diagnostic sense in medical records should be discontinued. In most cases a pathologic diagnosis can be made, and must be made if appropriate treatment is to be carried out. Since the treatment of stroke varies widely with the etiology, it is impossible to institute proper therapy without this information.

Subarachnoid hemorrhage arising from tumors or angiomas along the spinal axis is a special case in point.[1] The ready availability of information regarding the blood supply and venous drainage of these lesions has made possible surgical attack which previously was impossible. The application of microsurgery to the field of vascular lesions of the central nervous system is well under way and promises to keep pace with the progress made in angiography.

Michael P. Sperl, M.D.
St. Paul, Minnesota

*See page 805.

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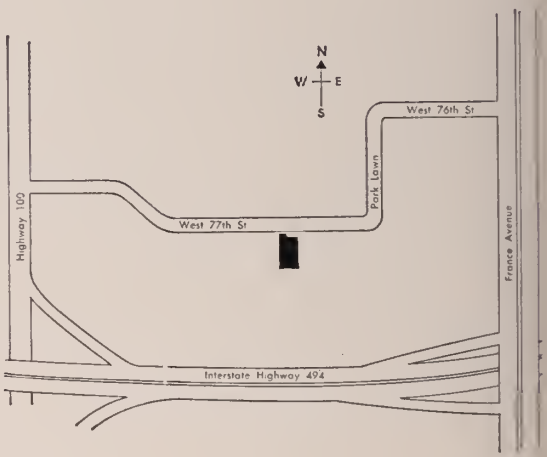
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Radiology and the Health Care Problem

In this period of critical re-appraisal of goals, systems and technics of health care delivery in general, Campbell* has ably and succinctly defined and discussed the major problems as they affect radiology services. He has explored new avenues for broadening the basis for providing both radiological services and recruitment of professionals and paramedical personnel into the field and has emphasized the need for realistic self discipline in cost analysis and control as preferable to third party control.

Campbell has not only stimulated us to think and act carefully in new frames of reference, but has also, characteristically, acted in response to his convictions. Foregoing his well established position as head of radiology at Indiana University Medical Center, he has accepted the challenging and uncertain hazards of developing radiological services and education in a large urban ghetto district.

In this age of belief in commitment to and self involvement in community needs, Campbell has set us an example to emulate. Although many of us may not agree entirely with some of the innovations he suggests or the experiments he conducts, he must be admired and congratulated on the courage he demonstrates in breaking with traditional ties in his effort to find new ways of ultimately providing more people with better health care.

George D. Davis, M.D.
President of Minnesota Radiologic Society

*See page 843.

Sino-Orbital Aspergillosis

Whereas clinicians are familiar with the often fatal outcome that follows sino-orbital infections with the genus Mucor in debilitated patients, they may not appreciate the fact that reasonably healthy individuals may become infected with the genus Aspergillum, which, though not fatal, is associated with a high incidence of visual morbidity. In his case report, Zinneman* has succinctly detailed the characteristic clinical presentation of sino-orbital mycoses. The physical findings of these somewhat uncommon infections are striking, and once seen, they are not easily forgotten. Saving the eye makes early consideration of the diagnosis of sino-orbital Aspergillosis particularly imperative. Prompt surgical intervention and fungus culture of debridement specimens will confirm the diagnosis and provide a rational basis for initiating definitive treatment.

Richard D. Hohl, M.D.
Minneapolis, Minnesota

*Zinneman, HH: Sino-orbital aspergillosis. Minnesota Med 55:7, 661, 1972.

University of Minnesota Postgraduate Medical Education

Proctology

The Division of Colon and Rectal Surgery of the Department of Surgery of the University of Minnesota Medical School in cooperation with the Minnesota Academy of Family Physicians will present a program in "Proctology" at the Nolte Center for Continuing Education on October 23-27, 1972. This program is conducted through the Office of Postgraduate Medical Education of the University of Minnesota Medical School. Fee: $160.00.

Letters to the Editor

Dear Editor:

The excellent article by Dr. Robert Rosenthal [February 1972] has what I assume is a typographical error—that is, in the sentence "The first of these was George Armstrong's Dispensary for the Poor Infants, opened in London in 1796." I am taking the liberty of sending you a photostatic copy of the front-piece of one of George Armstrong's writings which shows the date should be 1769 rather than 1796.

Hugh B. Lynn, M.D.
Rochester, Minnesota

Dear Editor

In reading the May issue of Minnesota Medicine* I noted with interest the article entitled "Laboratory Letter—Screening for Beta Hemolytic Streptococcus in the Throat" by Dr. C. W. Jarvis. There are some aspects of that article which I feel deserve comment. Dr. Jarvis advocates the use of 5-10% sheep blood in handling throat cultures for beta streptococci. The feature of beta hemolytic streptococci which physicians most often use in their office laboratories for identification is the beta hemolysis, and 10% sheep blood will fail to demonstrate hemolysis with certain group A beta hemolytic streptococcal strains. It is much more desirable, in order to use hemolysis as an accurate identification tool, to use 5% sheep blood. In addition, since streptolysin O is destroyed by oxygen, these plates should either be incubated in a CO_2 environment, or should have a small cut made in three or four appropriate locations on the plate in order to assure some subsurface growth of the streptococci with the resulting protection of the streptolysin O from surface oxygen.

Dr. Jarvis also suggests that physicians might purchase a few plates at a time from the nearest hospital bacteriology laboratory. This may not be the best advice. One can purchase sheep agar plates individually wrapped in plastic envelopes from several medium manufacturers where one is assured of a high degree of quality control, and quality control in many hospital laboratories is less than optimum with respect to the manufacture of media. Should a physician desire to buy a few plates at a time from a local manufacturer or from a local bacteriology laboratory one would hope that they would insist that the proper quality control procedures be carried out.

Dr. Jarvis indicates that human blood should not be used because this may inhibit the growth of streptococci. The reason for not using human blood is not because of the inhibition of growth of streptococci, but because human blood allows the growth of *Hemophilus hemolyticus* which may cause a confusing hemolytic reaction on blood agar plates from throat cultures. Sheep blood tends to inhibit *Hemophilus hemolyticus* and thus to minimize the aspect of confusion. In addition, it is often difficult to clearly differentiate alpha and beta hemolysis on human blood agar plates. Dr. Jarvis further indicates that beta hemolytic streptococci will not grow to within 15-20 mm of the bacitracin disc. Actually results on the kind of unstandardized situation which Dr. Jarvis advocates are very variable, and indeed many nongroup A strains will also not grow close to a bacitracin disc with a minimum inoculum. In addition, many group A strep, if a heavy inoculum is used, will grow down to within nine or 10 mm of a bacitracin disc. Bacitracin discs must also be carefully quality controlled in order to insure that potency remains. Whereas the method advocated by Dr. Jarvis has distinct advantages for the physician's office, the tenor of the article is such that the physician would be led to suspect that the above methods would give a high degree of accuracy, and such may not be the case.

John M. Matsen, M.D.
Minneapolis, Minnesota

*Page 467.

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phenobarbital (warning: may be habit forming)	(¼ gr.) 16.2 mg.	(½ gr.) 32.4 mg.	(¾ gr.) 48.6 mg.

Brief summary. Side effects: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma or urinary bladder neck obstruction as in prostatic hypertrophy. Contraindicated in patients with acute glaucoma, advanced renal or hepatic disease or hypersensitivity to any of the ingredients.

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Fifty Club

Owen H. Wangensteen, M.D.

From Amateur Accoucheur to Pigs to Professor of Surgery

THIS FIFTY YEAR CLUB member graduated with a Bachelor's Degree in Medicine in December 1921. At Minnesota, completion of an Internship then was mandatory for satisfaction of the M.D. degree. The writer came into medicine through the back door, through the portals of pigs and manure, a goodly spread of each. As a junior in high school my father had 50 sows that could not farrow their young. The veterinarian advised sending the sows to South St. Paul. During three weeks away from school all the sows, save two, were salvaged and approximately 300 piglets. I learned from the effort that a young boy's hand was superior to any instrument devised for the purpose. Thereafter my father insisted that I consider seriously becoming a doctor. However, my ambition was to be a farmer and a good one.

After three years in the College of Science, Literature, and Arts at the University of Minnesota and much manure hauling, loaded by hand in the hot summer of 1917, this Club member decided to capitulate to his father's wishes and to have a go at medicine. Much to my astonishment, I found the study far more agreeable than I had ever dreamed it could be. I came quickly to know that our language stands in great need of a word to connote transition from rejection to acceptance, a circumstance that touches all of us many times in a long life.

I had firmly decided to become an internist, but as a junior medical student (1920) on hearing the first lecture in Surgery from its Chairman, Dr. Arthur C. Strachauer, I decided before the lecture was over that surgery would be my career. That lecture persuaded me that the results of the ministrations in this discipline were more readily identifiable and more dramatic than those of the physician.

My stimulus to seek a career in academic surgery stemmed from my association with Dr. George E. Fahr, whose presence at the University in 1921 was like a gust of fresh, cool, and refreshing air into a smoke filled room. After completion of an internship at the University Hospital and a Surgical Fellowship during which I was privileged to have an exchange year at the Mayo Clinic, I became successively Instructor and Assistant Professor of Surgery. In the summer of 1927 at the urging of Dean Lyon and Dr. George E. Fahr, I took off for a study trip abroad which time was spent in Bern, Switzerland and visiting German, Viennese, Italian, English and Scottish surgical clinics. It was a unique experience. On my return in the Fall of 1928, I was made an Associate Professor and became the Department's Chairman in January 1930, after Dean Lyon and his search committee had sought in vain for an acceptable candidate. Two had been interviewed, Dr. Francis Newton from Harvard and the other Dr. Mont Reid from the University of Cincinnati, a trainee of Halsted's at The Hopkins. Both said to me in substance, "There is nothing here nor will there ever be."

Three years after assuming the Chairmanship, I ran afoul of our legendary and inspiring teacher in anatomy, Dr. Richard Scammon, then Dean of the Medical Sciences. However, J. Charnley McKinley, Acting Chairman of the Department of Medicine, who represented me in the discussions with Dean Scammon, Dean E. P. Lyon to whom I owed my appointment, Dr. Lotus D. Coffman, President of the University, and William J. Mayo, Regent, felt otherwise and my appointment continued uninterrupted.

Over the years a few opportunities came my way to go to other academic institutions with facilities and prestige the equal of or better than those which I enjoyed

at Minnesota. However, I felt that the University of Minnesota had treated me with kindly forebearance and I felt obligated to try to build a strong department worthy of the citizens of Minnesota. Moreover, the reprieve and the rare gift of a second chance were still in the foreground of my mind. Additionally, I was quite aware and conscious of the circumstance that an environmental atmosphere, unlike baggage, is not portable.

With the cooperative help of Dr. M. B. Visscher, Professor of Physiology, a large number of talented Surgical Fellows, skilled in operative surgery, gained training in the physiology of the circulation, an arrangement and situation that made it possible for a brilliant group of young surgeons to contribute greatly to the establishment of intracardiac surgery, one of the most significant contributions to medicine during my academic tenure.

Retirement came in June 1967, after 52 years of association with the University as man and boy. Dame Fortune had smiled kindly on my efforts; comfortable colleagues and good friends, who appreciated me far beyond my expectations and worth, made for me a very pleasant and rewarding career at Minnesota. Now after five years of retirement I find myself launched on a second career as an amateur historian of surgery attempting to trace the development of surgery, from the chaotic confusion of the pre-Listerian era, to its emergence as a scientific discipline.

My own work has been essentially that of general plumber of the alimentary canal. It has been my great privilege to be the regimental water carrier and the sideline cheerleader for one of the finest circles of talented and innovative surgeons gathered under one institutional roof in the 20th century. As the spokesman for this great orchestral band, I can only say, we are beholden to wonderful professional and interdisciplinary colleagues, to an approving and generous administration, and to the bountiful people of Minnesota, who have built here a truly great University, within whose walls and halls, the impossible can be achieved.

Request for Physican's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers has received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the Association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Because of limitation of space, pictures oriented horizontally are preferred. All pictures will be returned if identified with the name and address of the physician. Please submit your pictures as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 375 Jackson St., St. Paul, Minnesota 55101.

Farrell Stiegler, M.D.
Cover Editor

Viewing Box

Cystic Lung Lesion

C. R. McWILLIAMS, M.D. AND JAMES R. SCHUFT, M.D.

CHEST FILMS (Figures 1 and 2) are those of a 42-year-old Caucasian female.

The patient stated that she consulted a physician 14 months ago because of swelling involving her left foot. A physical examination at that time, including a chest Xray, revealed a spot on her lung. There was some question of tuberculosis and she was started on antituberculous medication. The symptoms regarding her foot subsided. Three months after the initial examination a chest Xray was repeated, revealing a slight increase in size of the spot on her right lung. The area in question had developed a cystic appearance.

Three months prior to her admission to the hospital, the patient stated that she developed the "flu" and has not felt well since then. She had a productive cough, had had intermittent hemoptysis and night sweats for the past two months and had had an eight pound weight loss.

The patient lived in the Los Angeles area for a number of years and made frequent trips to the San Joaquin Valley region. Physical examination revealed clubbing of all fingers and toes and mild swelling of both ankles. The physical examination was otherwise normal. The chest Xrays were obtained at this time. A needle biopsy of the lateral aspect of the right lung cyst was performed and

Radiologists, Magic Valley Memorial Hospital, Twin Falls, Idaho.



Figure 1



Figure 2

approximately 10 cc. of thick fluid was aspirated from the cavity. The material was examined by smear and culture. Hemophilus influenza was cultured from the aspirated material. Cultures for fungi revealed no growth during a four-week period. Cytological studies revealed no evidence of tumor cells.

Differential diagnosis: 1. Tuberculosis.
2. Non-tuberculous lung abscess.
3. Coccidioidomycosis.
4. Echinococcus cyst.
5. Neoplasm.

A thoracotomy was performed and the cystic structure, which was present within the superior aspect of the right lower lobe, was opened. Frozen section studies were made of the wall of the cystic structure revealing a poorly differentiated squamous cell carcinoma.

A right pneumonectomy was performed. There was no evidence of regional lymph node involvement. A nodular area in the apical region of the right upper lobe 1.5 cm. in diameter was sectioned and revealed the presence of a bronchiolar carcinoma. It was well differentiated and quite different histologically from the cavitary mass in the lower lobe.

The patient's chest films were reviewed and this right apical lesion could not be visualized, even when the "retrospectoscope" was used.

Final Diagnosis: Poorly differentiated squamous cell carcinoma.
Bronchiolar carcinoma.

I spent my shining hours washing faces, serving rations, giving medicine, and sitting in a very hard chair, with pneumonia on one side, diphtheria on the other, two typhoids opposite, and a dozen dilapidated patriots, hopping, lying and lounging about, all staring at the new "nuss," who suffered untold agonies, but concealed them under as matronly an aspect as a spinster could assume, and blundered through her trying labors with a Spartan firmness, which I hope they appreciated, but am afraid they didn't. Having a taste for "ghastliness," I had rather longed for the wounded to arrive, for rheumatism wasn't heroic, neither was liver complaint, or measles; even fever had lost its charms since "bathing burning brows" had been used up in romances, real and ideal. But when I peeped into the dusty street lined with what I at first had innocently called market carts, now unloading their sad freight at our door, I recalled sundry reminiscences I had heard from nurses of longer standing, my ardor experienced a sudden chill, and I indulged in a most unpatriotic wish that I was safe at home again, with a quiet day before me.*

---

*Louisa May Alcott: Hospital Sketches.

Iron therapy for anemia is almost as old as history itself



Celsus's empirical use of iron

Aulus Cornelius Celsus recommended an unusual form of iron therapy for the treatment of enlarged spleens—the oral administration of water that blacksmiths had used for dousing white-hot iron.

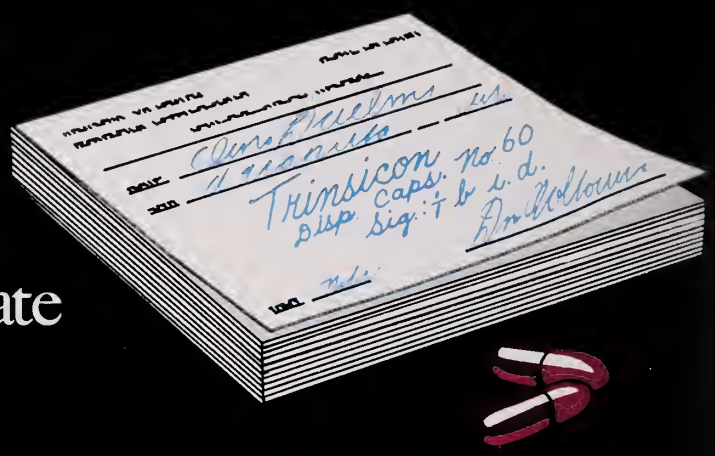
For more modern anemia therapy

Trinsicon®

Hematinic Concentrate with Intrinsic Factor

(See reverse side for prescribing information.)

Trinsicon®
Hematinic Concentrate with Intrinsic Factor



Description: Each Pulvule® contains—

Special Liver-Stomach Concentrate, Lilly (containing Intrinsic Factor)	240 mg.
Cobalamin Concentrate, N.F., equivalent to Cobalamin	7.5 mcg.
(The total vitamin B_{12} activity in the Special Liver-Stomach Concentrate, Lilly, and the Cobalamin Concentrate, N.F., is 15 micrograms.)	
Iron, Elemental (as Ferrous Fumarate)	110 mg.
Ascorbic Acid (Vitamin C)	75 mg.
Folic Acid	0.5 mg.

Indications: Trinsicon is a multifactor preparation effective in the treatment of anemias that respond to oral hematinics, including pernicious anemia and other megaloblastic anemias and also iron-deficiency anemia. Therapeutic quantities of hematopoietic factors that are known to be important are present in the recommended daily dose.

Vitamin B_{12} with Intrinsic Factor—When secretion of intrinsic factor in gastric juice is inadequate or absent (e.g., in Addisonian pernicious anemia or after gastrectomy), vitamin B_{12} in physiological doses is absorbed poorly, if at all. The resulting deficiency of vitamin B_{12} leads to the clinical manifestations of pernicious anemia. Similar megaloblastic anemias may develop in fish tapeworm (*Diphyllobothrium latum*) infection or after a surgically created small-bowel blind loop; in these situations, treatment requires freeing the host of the parasites or bacteria which appear to compete for the available vitamin B_{12}. Strict vegetarianism and malabsorption syndromes may also lead to vitamin B_{12} deficiency. In the latter case, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient.

Potency of intrinsic factor concentrates is determined physiologically, i.e., by their use in patients with pernicious anemia. The liver-stomach concentrate with intrinsic factor and the vitamin B_{12} contained in two Pulvules Trinsicon provide 1½ times the minimum amount of therapeutic agent which, when given daily in an uncomplicated case of pernicious anemia, will produce a satisfactory reticulocyte response and relief of anemia and symptoms.

Concentrates of intrinsic factor derived from hog gastric, pyloric, and duodenal mucosa have been used successfully in patients who lack intrinsic factor. For example, Fouts *et al.* maintained patients with pernicious anemia in clinical remission with oral therapy (liver extracts or intrinsic factor concentrate with vitamin B_{12}) for as long as twenty-nine years.

After total gastrectomy, Ficarra found multifactor preparations taken orally to be "just as effective in maintaining blood levels as any medication that has to be administered parenterally." His study was based on twenty-four patients who had survived for five years after total gastrectomy for cancer and who had been taking two Pulvules Trinsicon daily.

Folic Acid—Folic acid deficiency is the immediate cause of most, if not all, cases of nutritional megaloblastic anemia and of the megaloblastic anemias of pregnancy and infancy; usually, it is also at least partially responsible for the megaloblastic anemias of malabsorption syndromes, e.g., tropical and nontropical sprue.

It is apparent that in vitamin B_{12} deficiency (e.g., pernicious anemia), lack of this vitamin results in impaired utilization of folic acid. There are other evidences of the close folic acid-vitamin B_{12} interrelationship: (1) B_{12} influences the storage, absorption, and utilization of folic acid, and (2), as a deficiency of B_{12} progresses, the requirement for folic acid increases. However, folic acid does not change the requirement for vitamin B_{12}.

Iron—A very common anemia is that due to iron deficiency. In most cases, the response to iron salts is prompt, safe, and predictable. Within limits, the response is quicker and more certain to large doses of iron than to small doses.

Each Pulvule Trinsicon furnishes 110 mg. of elemental iron (as ferrous fumarate) to provide a maximum response.

Ascorbic Acid—Vitamin C plays a role in anemia therapy. It augments the conversion of folic acid to its active form, folinic acid. In addition, ascorbic acid promotes the reduction of ferric iron in food to the more readily absorbed ferrous form. Severe and prolonged vitamin C deficiency is associated with an anemia which is usually hypochromic but occasionally megaloblastic in type.

Contraindications and Precautions: Anemia is a manifestation that requires appropriate investigation to determine its cause or causes.

Folic acid *alone* is unwarranted in the treatment of pure vitamin-B_{12}-deficiency states, such as pernicious anemia. Indeed, the use of folic acid in large doses in pernicious anemia without adequate vitamin B_{12} may result in hematologic remission but neurological progression.

As with all preparations containing intrinsic factor, resistance may develop in some cases of pernicious anemia to the potentiation of absorption of physiological doses of vitamin B_{12}. If resistance occurs, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential and are recommended.

In extremely rare instances, skin rash suggesting allergy has been noted following the oral administration of liver-stomach material. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Hemochromatosis and hemosiderosis are contraindications to iron therapy.

Adverse Reactions: In rare instances, iron in therapeutic doses produces gastrointestinal reactions, such as diarrhea or constipation. Reducing the dose and administering it with meals will minimize these effects in the iron-sensitive patient.

Dosage: One Pulvule twice a day. (Two Pulvules daily produce a standard response in the average uncomplicated case of pernicious anemia.)

How Supplied: Pulvules Trinsicon® (hematinic concentrate with intrinsic factor, Lilly), in bottles of 60 and 500 and in Identi-Dose® (unit dose medication, Lilly) in boxes of 100.

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Lithium

BURTON P. GRIMES, M.D.

LITHIUM WAS IDENTIFIED as an element in 1818. is a light element with an atomic number of iree: an alkali metal of the sodium and potas- um group. In the 1940s it was used as a taste ubstitute for individuals who were on a salt-free iet. Unfortunately, the drug's toxicity included an ncephalitic syndrome which led to a number of atalities.[1,2] These fatalities attributed to lithium hloride) led to its withdrawal from the market.

Also in the late 1940s Cade in Australia noted thargy in guinea pigs following ingestion of lith- um. His clinical study of 10 manic patients was he first to suggest a psychotropic effect for lith- um.[3] A controlled study published by Schou in 954 demonstrated effectiveness of lithium in cute manic states.[4] Subsequently, the literature ontains detailed references to lithium metabolism, oxicity, use in prophylaxis and results in treatment f both mania and depression.

Methods

In order to use lithium in this country, one must irst have an investigation permit, then a source f the drug, and finally a means of measuring erum lithium levels. The dose of lithium carbo- nate is usually 0.3 gm to 0.6 gm. three times a lay. Blood tests are made at least twice weekly luring the initial control period. A level of less han 1.5 meq/liter is rarely associated with toxic manifestations.

From June 1967 until August 1970, we started a total of 54 patients on lithium (Table 1). The age range was 18 to 79; the average was 50.

Results

Two patients died. On autopsy we were unable to connect the deaths with lithium. One of the patients who died had pneumonia, and the other a myocardial disease. Four patients were discon- tinued respectively for polyuria, diarrhea, distance from the hospital, and transfer elsewhere for sur- gery. Three patients quit. Nine have been trans- ferred to other institutions or to care outside the hospital while continuing lithium therapy.

Address reprint requests to: Burton P. Grimes, M.D., St. Peter State Hospital, St. Peter, Minnesota, 56082.

Complications

Gastrointestinal

One 64-year-old man developed a severe case of diarrhea the first day he received a full dose of lithium. The diarrhea stopped several days after discontinuing the lithium. Transitory and rarely severe gastrointestinal symptoms are common dur- ing the first weeks.

Urinary

A woman on lithium treatment for depression discontinued lithium because of the development of urinary frequency.

TABLE 1
Summary of Lithium Carbonate Patients at St. Peter State Hospital

	N	%
Total patients started on Lithium	54	100 %
Total patients currently in the study and in the hospital[1]	23	42.6
Total patients lost in the hospital from the study and	2	3.7
Total patients lost from the study		
Discharged improved—to be continued on lithium[2]	16	29.6
Transferred improved to other hospitals	5	9.3
Discharged improved—d.v.* urinary frequency	1	1.8
Discharged improved—d.v. because of distance	1	1.8
Discharged from hospital—questionable improvement	2	3.7
Discontinued because of side effects	1	1.8
Discontinued for surgery	1+	1.8
Deaths	2	3.7
	54	100.0

[1]Includes one patient who was discharged to nursing home and returned.
[2]Includes one patient who was discharged, returned, and dis- charged.
+Had improved.
*dv—discontinued of own volition.

Neuromuscular

The patients in this study did not show significant neuromuscular abnormality during treatment with lithium. However, this is an important area of toxicity. Patients with a high blood level of lithium develop a gross muscular tremor, most obvious in its interference with writing. Tremor is an indication for immediate reduction of dose. Ataxia is also an early manifestation of a toxicity and likewise is an indication for lowering the dosage.

Thyroid

Three of the patients in this study showed an increase in T_4 levels which remained within normal limits. One patient became hypothyroid. These abnormalities with thyroid function have not been reported previously. A cause and effect relation is not definitely established in the patients we studied. Goiter has been reported to have developed in 12 of 330 patients,[6] but was not seen in our study.

Comment

The major benefit of lithium therapy is in the control of hyperactivity. This was apparent in 85 percent of patients we treated. It may be necessary to add other types of medication or perhaps electric shock to control acute hyperactivity until the lithium becomes effective. The majority of pa tients came under control within 10 days o starting lithium (Table 2).

TABLE 2

Percentages of 54 St. Peter State Hospital Patients Showing Improvement on Individual Target Symptom Rating Scales at Various Time Intervals During the First 30 Days of Treatment on Lithium Carbonate

Improvement Shown In:*	N	%
1-10 days	28	51.8
11-14 days	7	13.0
15-21 days	3	5.6
22-30 days	8	14.8
Variable, Questionable or No Improvement	8	14.8

* Improvement is taken as the point at which an individual's score on his individual Target Symptom Scale drops below the pretreatment level and either remains constant or continues to decrease for the remainder of the 30-day period.

Received 1970.

Another benefit is the lack of side-effects o maintenance. Manic patients have commented o the freedom from a feeling of fogginess whic they had experienced with the large doses o phenothiazines they had required on previous epi sodes. There is also a longer interval betwee attacks. While manic attacks are ordinarily recur rent, the patient can expect several more symp tom-free months between attacks while on lithiun than with any other mode of therapy. For exam ple, the control of hostility while taking lithiun has made it possible for one patient to be out o the hospital successfully for two years. She ha re-established relationships with her family and i living and working out of the hospital.

The control of hostility is particularly importan in the nursing care and supervision of the patient With lithium therapy, the improved social adjust ment in the hospital makes life much mor pleasant, not only for the patient, but for all th hospital personnel.

The cost of treatment is measured in terms o periodic supervision while on maintenance ther apy in the community. Laboratory costs will in clude monthly or more frequent serum lithium levels; the cost for equipment to determine serum lithium should be less than $1,000. The thyroid activity should probably be measured at two-month intervals. Lithium salts are all inexpensive and should not be a financial burden if they are released for general use.

For further details on the use of lithium carbonate for manic depressive states consult references six to eight.

Summary

Fifty-four patients were started on lithium for the control of manic and/or depressive reactions. Definite improvement was seen in 85.2% of the patients.

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Fracture Conference

Ankle Fractures

JOE L. NETTLES, M.D., JOHN A. ELSTROM, M.D. and
EINER W. JOHNSON, JR., M.D.

Dr. Joe L. Nettles:

Percival Pott of London in 1769 has been credited with the first attempt at the description of the mechanism of fracture-dislocation at the ankle, with its associated ligamentous injuries. Dupuytren, in 1816, and Cooper, in 1822, pointed out the significance of talar motion and its relation to the malleoli as the force that initiates ankle injuries. Maisonneuve, in 1840, however, was the first to appreciate that external rotation of the foot around the vertical axis of the talus is a major etiologic factor in these injuries. Expansion and modification of this work, by Ashhurst and Bromer[1] in 1922, Lauge-Hansen[2,3] in 1948 and 1952, and Burwell and Charnley[4] in 1965, have further defined the individual components of ankle injury.

Two cases of ankle fractures will be presented with the purpose of discussing their nature and its relationship to treatment.

Case 1

Dr. John A. Elstrom:

A 44-year-old salesman was injured when a cow fell on his left leg. Examination in the emergency room at admission showed an obvious deformity of the ankle. Circulation and sensation were intact.

Dr. Charles F. Mess:

The Xray revealed a vertical fracture of the medial malleolus from the level of the ankle mortise (Figure 1 *A* and *B*). The lateral malleolus was also fractured at the level of the ankle joint. This appeared to be an unstable fracture.

Dr. Nettles:

The fracture, tested under anesthesia, was grossly unstable. It was so unstable that it would not respond to closed methods, especially the vertical fracture of the medial malleolus.

Dr. Mess:

For reduction, two screws probably should have been used to counteract any rotational forces, as the medial fragment looked large enough to adequately accept a screw.

Dr. Nettles:

We used one screw and a Kirschner wire at operation, because we thought that the medial malleolar fragment was too small to tolerate a second screw. We also used a Rush pin at the lateral malleolar fragment (Figure 1 *C* and *D*). The patient subsequently has done well. We removed the Kirschner wire at three weeks because it was causing some irritation. At the end of two months, healing had obliterated the medial fracture line.

Case 2

Dr. Elstrom:

A 49-year-old construction worker was struck by a piece of steel and sustained an open injury to his left ankle. He was brought to the emergency room approximately 30 minutes after the accident (Figure 2 *A* and *B*).

Dr. James J. Haven:

This patient had a severe fracture dislocation of the ankle; the medial malleolus was fractured horizontally at the mortise. The fibula was fractured fairly high up, and there was diastasis between the tibia and fibula.

Dr. Nettles:

Dr. Buckley, do you differentiate the types of diastasis seen in ankle fractures?

Dr. John P. Buckley:

Yes, there are two varieties. *Classic diastasis* is considered a separation of the fibular shaft from the tibia; whereas *interosseous diastasis* between the two fibular fracture fragments at the level of the joint is probably just as significant clinically and may allow lateral displacement of the talus.

Dr. Nettles:

The fracture was a compound one. The articular surface of the tibia was exposed (Figure 3 *A*) and the medial malleolus was sheared off. The patient was taken to the operating room for a thorough debridement of the wound. The medial malleolar fragment was restored to its tibial "seat," and the dislocation was reduced very satisfactorily (Figure 3 *B* and *C*). The torn posterior tibial tendon was repaired. We elected not to fix the lateral fracture because of the severity of the open injury and the risk of infection if further incisions were made. The wound was closed over a Penrose drain (Figure 3 *D*). The patient did well.

Dr. Einer W. Johnson, Jr.:

His wounds healed nicely. However, he had several superficial abrasions across the anterolateral aspect of his leg, and these took a while to heal. We were worried about the external malleolus. I thought that once the

Doctors Nettles and Elstrom are Residents in Orthopedic Surgery, Mayo Graduate School of Medicine (University of Minnesota) Rochester.

Dr. Johnson is a Consultant, Department of Orthopedics, Mayo Clinic and Mayo Foundation.

Fracture Conference held July 7, 1969.

medial malleolus was fixed the external malleolus would fall into line, but that did not happen. Ultimately, three and one-half weeks after the initial treatment, a Rush nail was placed up the external malleolus, which gave an adequate reduction of the mortise (Figure 4 *A* and *B*).

Dr. Mark B. Coventry:

The fibula was not posterior, was it? This can happen. The lateral malleolus will be displaced posteriorly, and this positioning may escape recognition.

Dr. Johnson:

No, the lateral malleolus seemed to be locked, ju the way it looks in Figure 3 B, with the distal fragmer pushed medially and held by the proximal fragment. Fr quently, lengthening the malleolus enough to get it r duced after three weeks is difficult.

Discussion

Dr. Richard S. Bryan:

Interestingly, in these two cases, the mechan



Fig. 1 (Case 1)—Bimalleolar fracture of left ankle. (A) and (B) before reduction. Anteroposterior (A) and lateral (B) views. (C) and (D) After open reduction and internal fixation.

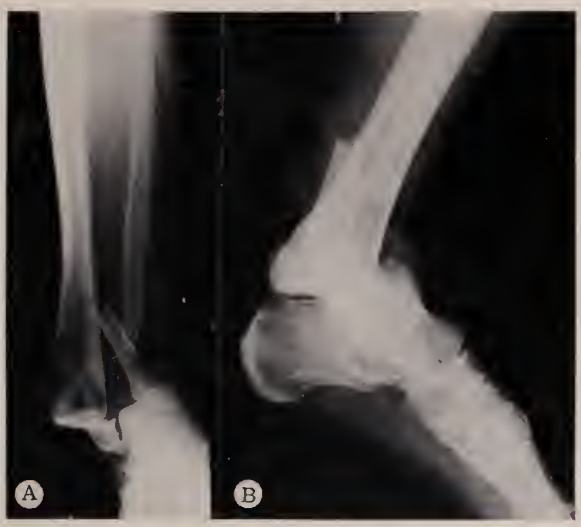


Fig. 2 (Case 2)—Open fracture-dislocation of left ankle. (A) Anteroposterior view. (B) Lateral view.



Fig. 3 (Case 2)—Open wound of fracture-dislocation. (A) At admission. (B) and (C) After debridement reduction and internal fixation of medial malleolar fracture. Anteroposterior (B) and lateral (C) views. (D) Wound after closure over Penrose drain.

ism of injury was the opposite. In the first case, it was supinated, and in the second, the foot was pronated.

Dr. Nettles:

Ashhurst and Bromer,[1] while pointing out the significance of the work of Maisonneuve, first attempted to classify fractures in relation to their causative mechanism. Subsequently, Lauge-Hansen,[2,3] and Burwell and Charnley[4] have further refined this classification (Figure 5). They divided the injuries into five categories.

Supination-lateral rotation fractures are produced by lateral rotation of the supinated foot. The talus rotates against the lateral malleolus first, rupturing the anterior tibiofibular ligament. Subsequently, a spiral or oblique fracture of the lateral malleolus occurs at the level of the ankle mortise. Further lateral rotation either ruptures the posterior tibiofibular ligament or fractures the posterior malleolus. The originally relaxed medial deltoid ligament finally comes into stress, resulting in a tear of the ligament or, more commonly, in a fracture of the medial malleolus.

Pronation-lateral rotation injury is the most common. In this situation the foot is in an attitude of pronation. The deltoid ligament, which is under tension, either ruptures or pulls away the medial malleolus in the first stage. Then the anterior tibiofibular ligament and the interosseous ligament are disrupted at the second stage, followed by a fracture of the fibula, typically three inches or more above the ankle joint. Ultimately, further rotation can produce a posterior fracture at the posterior tibial margin.

A supination fracture, or the supination-adduction fracture of Lauge-Hansen, can be considered an inversion fracture. This begins with a traction fracture of the lateral malleolus at or below the level of the ankle joint. Then the talus exerts enough pressure on the medial malleolus to fracture it, usually almost vertically, as the talus shifts into adduction. Vertical disruption of the medial malleolus is characteristic of the supination fracture.

The pronation or abduction fracture is also referred to as an eversion fracture. There the first stage is either a rupture of the deltoid ligament or a break of the medial malleolus. Then pressure of the talus against the fibular produces a typical fracture through the fibula, slightly above the ankle joint. There is usually a small comminuted fragment on the lateral portion of the fibular fragment by which this type of injury can be identified. In fact, according to Burwell and Charnley,[4] this is the advantage of the classification: one can understand the mechanism of injury by looking at the level of the fibular fracture or at the type of fibular fragment.

A fifth category, very uncommon, is a *comminuted distal tibial and fibular fracture* due to a fall from a height.

Lauge-Hansen[2,3] developed this classification to help him in his closed treatment of ankle injuries with very good success. However, Burwell and Charnley[4] have taken the same etiologic classification and used it in their advocacy of the open-type or surgical treatment. Recently they[4] reviewed a series of 137 fractures, about 98% of them falling into these categories, with most of the patients being treated by open reduction with internal fixation. Eighty-two percent had good results; 14%, fair results, and 4%, poor results. There were six instances of infection, five of them minor.

Burwell and Charnley also pointed out the *disadvantages of closed treatment* of these fractures: (1) the difficulty in achieving and maintaining accurate reduction, (2) the duration of immobilization, and (3) the frequency of malunion or nonunion. After internal fixation, they do not apply plaster. They leave the wound exposed and encourage active exercise of the joint. After two or three weeks, when active motion of the joint has been obtained, the patient is placed in a walking cast for about five weeks.

Dr. Coventry:

I think that you must know the mechanism of injury and the forces pertaining before you can accurately reduce the fracture and hold it. The key is probably the medial malleolus. We have overemphasized this because there are some patients in whom the medial malleolus has been reduced but in whom the ankle mortise is still widened. We have to look at the interosseous membrane because, if that remains spread, the result will be poor. Any diastasis has to be reduced.

Dr. Nettles:

Would you fix the interosseous membrane? Would you put any kind of fixation across the two bones?

Dr. Coventry:

Yes indeed, if it is separated and cannot be

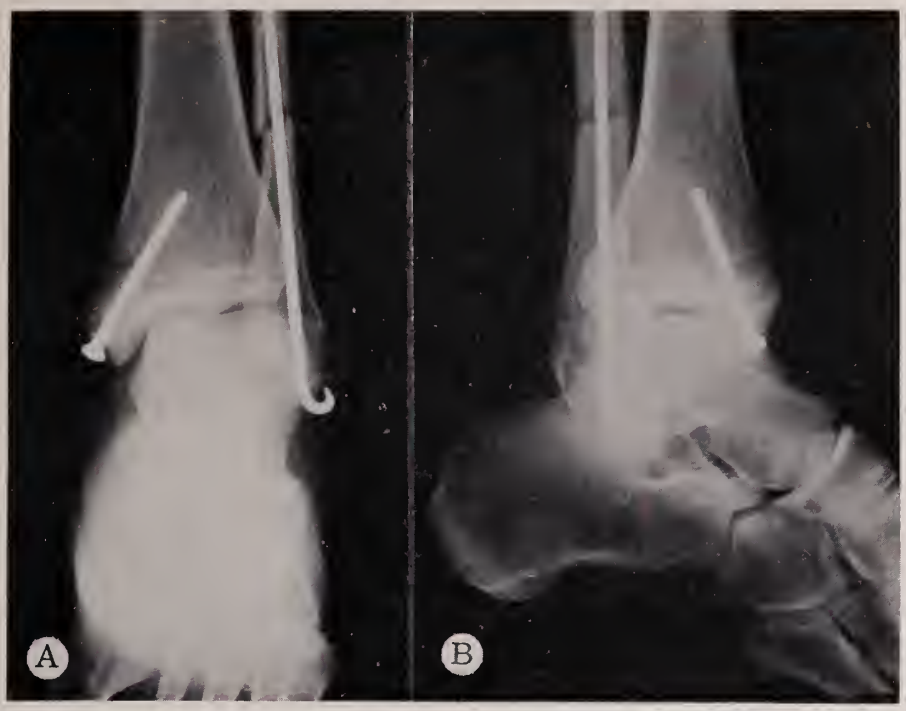


Fig. 4 (Case 2)—(A) and (B) After internal fixation of distal fibula with Rush pin for correction of distal tibiofibular diastasis.

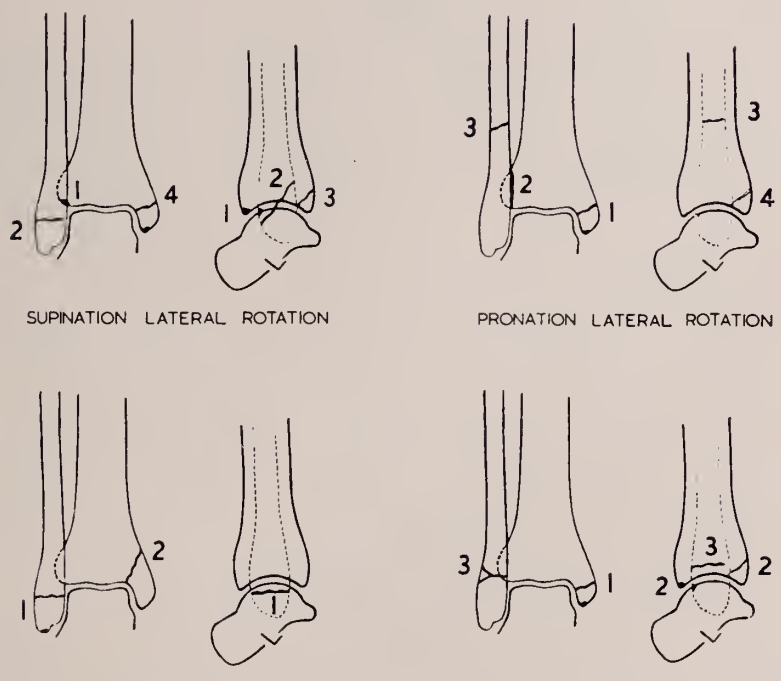


Fig. 5—Four common types of fracture in Lauge-Hansen classification. (From Burwell, H. N., and Charnley, A. D.: The Treatment of Displaced Fractures at the Ankle by Rigid Internal Fixation and Early Joint Movement. J Bone Joint Surg [Brit] 47:634, 1965. By permisison.)

reduced any other way.

Dr. Nettles:

Burwell and Charnley[4] have stated that they rarely put a pin across the two bones.

Dr. Coventry:

What do they do if they have a separation?

Dr. Nettles:

They maintain that if the injury to the malleolus is reduced and stabilized, the diastasis is also reduced and will be maintained in proper position. They further point out that in their series, although classic diastasis occurred in 24 patients, it was not always visible on Xray.

Dr. Bryan:

One point should be made: if you put a screw from the fibula into the tibia, you should be very cautious about having the patient walk, whether he is in or out of a cast, because the screw will break. The screw must be removed, usually at about six weeks.

Dr. Joseph M. Janes:

I think the vertical compression fractures at the lower end of the tibia are difficult to treat by open reduction. Often they can be treated by putting a pin through the os calcis, placing the extremity on a "Bohler frame" for traction for several weeks until the fracture is secure then putting the extremity in a cast. But opening up the lower end of the tibia to provide internal fixation is an almost impossible situation, because of the great degree of comminution.

Dr. Nettles:

In conclusion, these two cases demonstrate the importance of discovering all the injuries in an ankle fracture. From an informed evaluation of the roentgenogram, the individual components of an ankle injury in their correct time sequence can be determined and the presence of intermediate ligament injuries inferred. The evaluation can be further supplemented by examination under anesthesia with stress films and by arthrography.

As Ashhurst and Bromer[1] have stated: "It is perhaps unnecessary to argue the desirability of classification; for, without classification, the relation of one lesion to another can be neither remembered nor understood in any department of knowledge; and comprehension is a prerequisite for intelligent memory and for rational diagnosis and treatment." Finally, Burwell and Charnley[4] have pointed out that accuracy of reduction is probably the major factor in the prevention of subsequent arthritis of the ankle.

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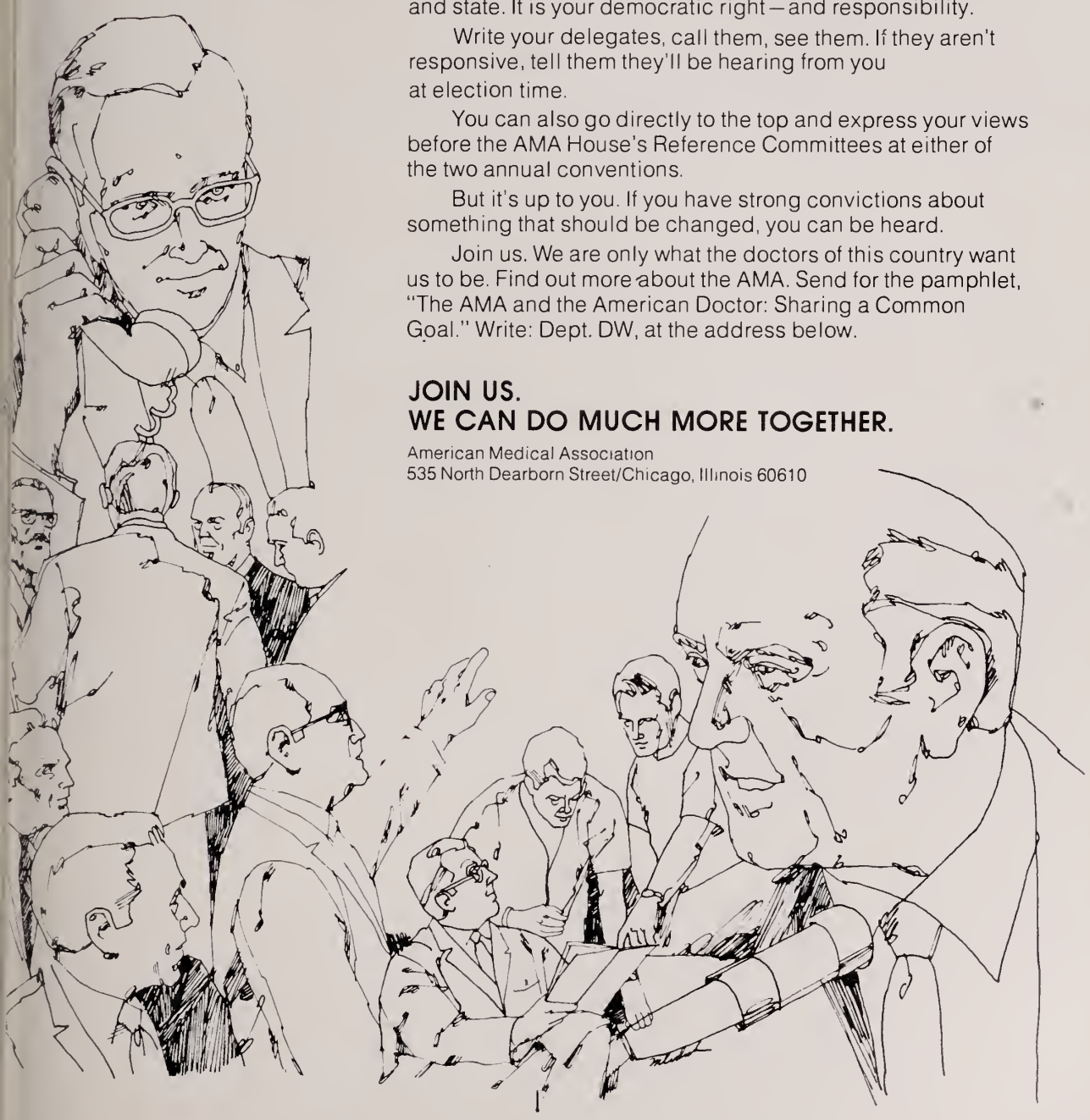
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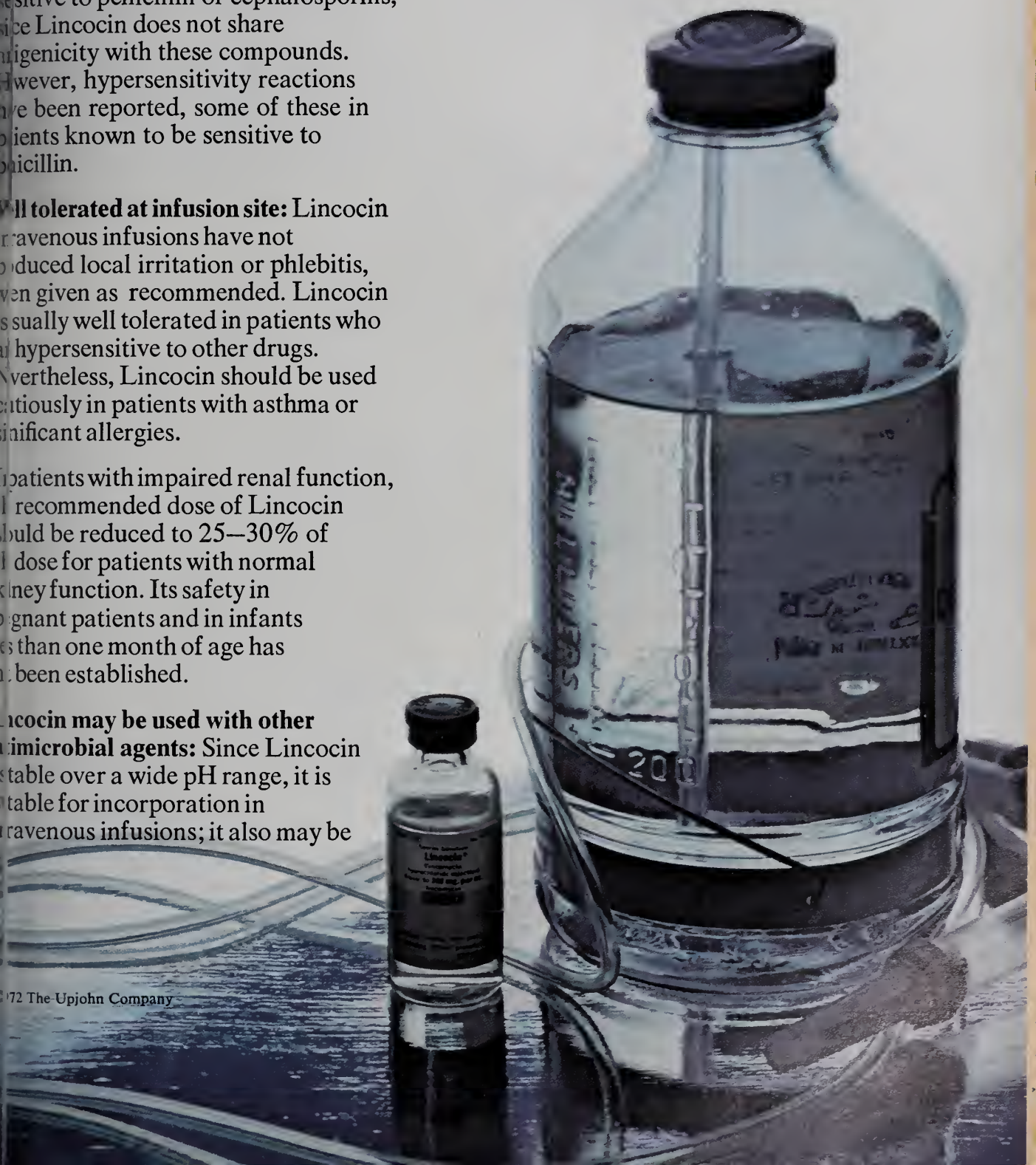
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Special Article

Radiology and the Health Care Problem

JOHN A. CAMPBELL, M.D.

"The guest can better judge the feast than the cook"—Aristotle

NO SINGLE LEVEL of our medical system is untouched by the push toward change. The call for change is motivated in five basic areas: people, money, medical facilities, doctors, and medical education. All of these affect radiologists.

People Problems

An ever enlarging group of citizens are obsessed with the fact that in the world's richest society which spends $400 per person annually on defense and only $13 per person on health, there are millions of citizens unable to obtain a reasonable level of medical care at reasonable costs.

Dr. John Knowles[1] of Massachusetts General Hospital dramatizes this in the following statements: "The financial gap is considerable when one realizes that there are 45 million of our 200 million population who qualify as poor with incomes of less than $4345 per year for a family of four. About 25 million of these 45 million impoverished citizens are living in cities, and the other 15-20 million still live in suburban or rural areas. The quality of their lives is marginal at best and their health precarious. Lack of adequate nutrition, schooling, jobs, housing, civil rights and transportation limits their ability to achieve health care in the fullest sense of the word. Lack of health education along with financial and geographic barriers which limit access to physicians and health institutions deny them the necessary medical services received by the other 155 million people of the country. As our per capita cost of hospitals, doctors, and drugs increases, more of the marginal group are driven into further medical indigency, and more of the middle class people join in their plight. When more and more people wonder why they have such difficulty getting the excellent care which we have developed, something is apt to happen, and let's hope it doesn't require a destructive type of confrontation that denial of other preceived rights have produced lately." Economist Pollack[2] goes a step further and feels that all or virtually all Americans are now to be considered medically indigent, and that some form of indemnification for all has become a necessity.

There is another factor. Medical care is no longer regarded as a privilege. Health is considered as much a human right as is education. Yet medicine is the only big business where the consumer has no control over what he buys. Since health care is a tight monopoly, it seems destined to become a public utility and we will obviously need to accept regulations to develop the proper social-scientific institution capable of meeting whatever goals are desirable. We can ill afford to defend the status quo on the grounds that health insurance based on group practice or prepayment plans is the opening wedge for government control of medicine. In fact, it is the surest safeguard against such an eventuality.

We radiologists have not really defined our goals of health care. Can we continue our pursuit of excellence and deliver good radiology to all the people? Or will we need to accept mediocrity to some extent? There is need for research in developing simplier, faster, and more available radiological services to patients and physicians alike. One idea is to eliminate out-patient services in hospitals and having practicing radiologists of the community furnish these in offices and multipurpose regional clinics. Another is home health care as a substitute for some hospital care, but including basic radiologic and laboratory work done by shuttle vehicles.

The shortage of radiologists must be met by

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See editorial, page 821.

the more liberal development of paramedical personnel and other schemes to increase the efficiency of those available. The radiologist should participate in the better distribution of radiologic care throughout the community by taking responsibility for certain population or geographic areas, offering services to deprived areas, and developing cooperative types of coverage. He should make a stronger effort to recruit as trainees in service programs blacks, the poor, foreign born and others not like himself. At Indiana University, I have utilized an increasing number of uneducated, hard core unemployed, with great success in jobs as orderlies, housekeeping, equipment maintenance, and technician assistants. Because of advanced age, alcoholism, and no previous employment records, these people were rejected by our employment office, and hired only as my personal responsibility. I have found them more compassionate with patients than younger employees, to have better attendance records, and to be tremendously grateful and loyal. Only one has dropped out, and two have advanced into more responsible departmental jobs. Employment of these persons is well worth the efforts required, and constitutes a form of community health care in itself.

Money Problems

Total health care expenditures in the United States will rise from 60 billion to 65 billion by the end of 1970 and to over 100 billion by 1975 to become the nation's biggest industry. Of this 60 billion, about two-thirds are generated in the private sector, and the remainder from government money. About 22 billion of the total or one-third of the health dollar is spent for hospital care, 12 billion for physician fees, and six billion on drugs. The average per capita cost of medical care in 1969 was $400, and the average patient's hospital bill $515. Health care presently accounts for 6% of our gross national product, and will consume 8 to 10% of all personal income by 1975.

Hospitalization costs are currently running as much as $100 per day in many places as compared with an average of $32 in 1960, and only $15 in 1950. If this rate of increase persists, costs of $500-$700 are predicted by the year 2000. Knowles[3] indicates that costs for intensive care beds at Massachusetts General Hospital are averaging $300-$500 per day now and could rise to $1,000 per day by 1980.

The predominant method of payment of medical care today is through third parties, meaning private, industrial, or government insurance. These will cover about one-third of patient medical expenses in 1970. One problem with them as pointed out by Dr. Eugene A. Stead, Jr.[4] is that the third party system does not provide an incentive for either the patient or physician to make costs less. Stead feels solutions for this must be new, and that they cannot come from reworking old institutions. He also feels that a national payment plan through Social Security is not going to work. The cost of medicare has increased from 3.2 billion to 8 billion, while medicaid from 1. to 5.5 billion since 1966. Pouring billions into the solution only forces costs upward and brings on more rebellion against them. He advocates that this problem be given the attention of economists, sociologists, and politicians in seeking a fresh creative solution. Another problem is that sickness or hospital insurance is not true health insurance, and covers only about 35% of the total medical expense, so that for chronic illnesses even the fully insured is in trouble. Moreover it furnishes too few benefits for office services, radiology, laboratory, and drugs outside the hospital.

One newer approach which is said to lessen over-utilization and unnecessary procedures, is the prepaid group practice plan. For hospitalization, insurance tallied 876 patient days per thousand subscribers as against 408 per thousand for the group practice plans, while for surgical procedures insurance showed a rate of 83 per thousand while prepaid groups had 31. For tonsillectomy the ratio was almost 8:1. Group practice and prepayment plans are growing, with about 2500 such multiple specialty groups now formed, some in big cities, some in small towns, some in hospitals, some in large medical centers, and some in a simple suite of doctors' offices. The combination of hospital based group practice with prepayment on a district basis in cities or regional basis in rural areas is said by Dr. Russell Lee[5] to be twice as efficient a way of delivering medical services as a present system of fee for service in the single doctor-patient pattern. It will probably take multiple systems to fulfill our needs, and some degree of competition between these may be in the patient's best interest. Radiologists should be free to select whatever scheme best

erves their effective role in the community, rather han by prescribed edict. The radiologist should lso increase his empathy for the patient by re-earching every conceivable means of improving ervice at less cost. Discipline in this area must e exercised whether or not fees are covered by hird parties.

Medical Facility Problems

Lee[5] has estimated that 30% of patients in a ospital at any one time should not be there. his over-utilization results from admissions for hat are really diagnostic procedures to gain nsurance, or the retention of patients past the cute stage of their illness. In addition, the ational shortage of 200,000 nurses has actually orced the closing of many hospital beds. All of hese problems affect hospital radiology depart-nents, causing peak loadings, uneven patient low, uneconomical emergency coverage and in-fficient equipment utilization. Radiologists have responsibility not to over-equip hospitals with liagnostic and therapy units for which there are oo few patients or no specialists who can use heir yield. We have many more cobalt units han we have available radiotherapists. Most of ll, radiologists have an obligation to work to eliminate unnecessary radiologic utilizations.

At Indiana University we have combined the radiotherapy facilities of five hospital units, and patients are shuttled to and from this depart-ment. We are suggesting combining the emer-gency services of these same hospitals (2000 beds) to avoid the costly duplication of equipment and on-call manpower. Patients destined for state, federal, county, or private units would be transferred to their respective hospitals after emergency services are completed. Teams of emergency physicians representing radiology, sur-gery, orthopedics, medicine and pediatrics will manage the emergency area around the clock. The service facilities of the other units will handle only elective radiology during regular hours. Radiologists should also tailor their serv-ices to expedite patient care and shorten both out-patient and in-patient stays. This may require abbreviated reports, reliance on paramedical peo-ple, staggering off-time to insure full services on week-ends. Finally the radiologist should employ broader use of systems analysis[6] in exploiting the tremendous technological advances to increase health manpower productivity and to improve the service yield of his department.

Doctors' Problems

Doctors deny responsibility for the patients' health care dilemma on the grounds of the physician shortage, excess patients, faulty patient attitudes, hospital policies, and the harrassment or interference from third parties. They point out that the problem is a reflection of the qualities of the consumption-oriented, impersonal society in which it develops; that doctors treat the poor with more common humanity than society as a whole; that if the physician makes a good income is he not merely doing something that is praised in every other line of endeavor? These arguments are true. Yet the public counters with equally logical questions. Should the physician not be urging his organizations to liberalize their views on socio-economic matters? Do new delivery sys-tems really threaten the financial security of the doctor? Or is his security more jeopardized by a society deprived of a better delivery system? It is difficult to be objective about a problem in which one has a vested interest, so radiologists should welcome the participation of the con-sumer, policy makers, and other experts. We should welcome the exposure of our inadequacies if we sincerely wish to correct them.

Radiology personifies the manner in which atomization of the huge body of medical knowl-edge today has made doctors inextricably depend-ent upon each other to produce good medical care. Doctors prefer to practice where there is good radiology. Hence a better supply and dis-tribution of radiologists is one of the keys to the better distribution of health care. With a short-age of radiologists, the centralized type of medical care predominates. Adequate numbers backed by paramedical teams could break one of the bottle necks of care distribution.

Educational Problems

The development of primary, first contact, continuing medical care is commanding the energy and priority of nearly every medical school in the nation today as it seeks to meet public de-mands for physicians. The university has the compelling responsibility to develop the basic science of health care hand in hand with educa-tion. Health care research is the evaluation of the outcome of such endeavors. Haggerty[7] has likened this field to the task of trying to put a river bank on a swamp. Medical schools face staggering financial problems and the galloping

advance of technology contributes to these.

As pointed out by Spellman,[8] medical students have recognized earlier than many of us one of the fundamental phenomena of our society. This is the observation that within the academic community, the medical school stands at the interface between the revolutionaries and the designated beneficiaries of their fervor, the poor and the black. Dr. Martin Cherkasky, Director of Montefiore Hospital, adds: "there is now a substantial number of medical students who don't put economics above everything else. These young people want to find in their profession a social commitment as well as a decent living. They are beginning to force changes in the curriculum. They don't think that molecular biology is more important than people."

During the past decade drastic curriculum changes have been made aimed at a greater production of graduates. Indiana University is embarking on a plan to eventually double its present enrollment of over 225 students per class by utilizing other university-community-hospital complexes in the state. The biomedical facilities of other universities in the state will be used to teach core groups of 50 first year medical students. These groups will transfer to the Indiana University medical school during the second and third years to finish core training and select specialty tracks, return to their satellite school for a fourth clinical year. All of these programs give a much needed flexibility to medical education and for the first time will permit students a choice of pathways or tracks through medical school.

Medical students will graduate with highly specialized and differentiated educations. The young prospective radiologist may have two full years of course work in radiology beyond time alloted to these subjects in the core curriculum by the time he graduates. These students are obviously unsuited for the medical graduate programs currently offered. They would not only be able to by-pass the internship and enter directly into residency, but with advanced education they will no longer need the three or more additional years as residents. This period could be shortened considerably. Indeed it may be advisable for residency programs to have no set length but be flexible enough to allow the usual variations in preparation and competence. The certifying boards would specify the curriculum requirements of such track students, and determine their competence for practice by examination. Carrying this a step further, the granting of state or national license to practice could be automatic on receipt of board certification and regulated only on the basis of opportunity.

Another source of manpower in medicine are the graduates of foreign medical schools, many of whom are the growing numbers of students rejected for admission to U.S. schools. Some 3000 Americans, equivalent to seven averaged sized U.S. medical schools are currently enrolled in foreign schools. We have 40,000 foreign educated physicians practicing in the U.S. today. In 1966-67, the number of foreign medical graduates, many of them U.S. citizens entering this country outnumbered graduates of U.S. schools 8540 to 7743. This indicates no shortage of potential applicants for expanded U.S. schools.

It is hoped that these track programs will permit schools to vastly increase their number of graduates. At the same time, there is great need to develop clinical support systems in the form of paramedical assistants. These range from formal university programs to apprenticeship-like instruction of selected candidates who usually possess certain basic qualifications in the medical field such as military corpsmen, radiologic technology, or nursing education. One important advantage of apprentice-type training is that it can be carried out in any radiologist's office. Our own experience has been to train our advanced radiologists to be administrative assistants, librarians, coding and retrieval personnel, photographic illustrative technologists, and special procedure technologists in gastrointestinal, chest, angiography, and urography.[11] These assistants actually perform all or part of the entire technical procedure thus releasing the radiologist to give more of his time to consultation and diagnosis. Others have trained technological assistants in the actual preliminary interpretation of roentgenograms of certain areas which lend themselves to the decision tree-type of interpretive approach as devised by Tuddenham.[12] In this way technologists can presort films of the chest, gallbladder, colon, and skeletal systems into normal and abnormal groups and thus simplify secondary readings by radiologists.

Another extension of the core track type of

nedical education is the concept of endless con-inuing education for the graduate. This would ›e achieved by requiring the radiologist to return o medical school in a full-time refresher-teaching ·ole periodically in order to sustain his licensure. During this sojourn at the school his practice would be continued by an advanced resident or ›ther faculty member. Many of these changes in he production of health professionals call for ong overdue revision and updating of our licen-sure laws. License to practice medicine should ›e based on competence in field examined, and he bottlenecks of credential requirements should ›e eliminated.

Conclusions

The radiologist cannot possibly escape the coming confrontation with the people seeking an improvement in the delivery of health care. The answer is change, and the radiologist must help to shape it.

He must work to make his services more available to people, to help solve the problems of cost, to prevent the over-utilization of radiologic procedures, to transfer out-patient services from hospitals to other community facilities, to help teach radiology to more students and health professionals, to create effective community-wide emergency services in radiology, to facilitate the broader development of paramedical personnel, and to be less competitive and more cooperative with others in the field.

This may well be the opportunity for the radiologist to discard many of the anachronisms of the past. Certainly the cure would seem less painful than the disease.

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University of Minnesota

Course on Recent Advances In Infectious Diseases

The Department of Medicine and the Office of Postgraduate Medical Education of the University of Minnesota announce a course "Recent Advances in Infectious Diseases" to be held at the Mayo Memorial Auditorium on the Minneapolis Campus October 12 to 14, 1972 in honor of Wesley W. Spink, Regents' Professor of Medicine and Comparative Medicine.

The course will offer recent information on detection, management and prevention of serious infectious diseases in man. It will include a broad view of the biology of infectious agents and host responses. Several related clinical problems in each of five general topics will be reviewed in depth. Topics will include Gram-negative Sepsis, Pyogenic Infections, Zoonoses, Respiratory and Streptococcal Disease and Immune Deficiencies. There will be time for questions and several panel discussions. The course is designed for physicians engaged in the practice of general medicine and the clinical management of infections in children and adults. The tuition is $125.00. Residents and fellows-in-training $80.00.

Further information may be obtained from James M. Schless, M.D., Director, Postgraduate Medical Education, University of Minnesota Medical School, Minneapolis, Minnesota 55455.

Minnesota Health Professionals Honor Congressman Ancher Nelsen

CONGRESSMAN ANCHER NELSEN was honored for his efforts and leadership in the area of health legislation by Minnesota health science professionals at a special appreciation dinner on July 31, 1972. About 500 men and women representing medicine and other health related fields attended the bipartisan affair which was held at the Radisson South Hotel in Bloomington.

Speaking at the dinner was HEW Secretary Elliot L. Richardson who praised Congressman Nelsen for his efforts in influencing the passage of sound health care legislation. Richardson stated "his (Nelsen's) influence and prestige on Capitol Hill springs not from headline grabbing flamboyancy, but from patient, constructive and above all tireless work."

Nelsen is currently serving his seventh term in Congress representing Minnesota's Second District, and is the ranking Republican on the Public Health and Environment Subcommittee of the House Interstate and Foreign Commerce Committee.

Another speaker, Congressman Paul G. Rogers (D), Florida, and Chairman of the Public Health and Environment Subcommittee, gave high praise to Nelsen and stated: "he is doing a magnificent job."

Doctor Lyle French, Vice President for Health Sciences, University of Minnesota, served as Dinner Chairman and Doctor Ray Pruitt, Dean of the Mayo Medical School, acted as Master of Ceremonies.

Other headtable guests included: John Zapp, D.D.S., Assistant Secretary, Department of HEW, MSMA President George B. Martin, M.D. and Mrs. Martin and representatives of other sponsoring organizations.

Congressman Nelsen's daughter, two sons and their spouses, and his sister attended as special guests.

Joining the Minnesota State Medical Association in this recognition dinner for Congressman Nelsen was the Minnesota Nurses Association, Minnesota Dental Association, Minnesota State Pharmaceutical Association, Minnesota Hospital Association, Minnesota Veterinary Medical Association, Mayo Medical School, Mayo Foundation and the University of Minnesota Health Sciences.

Harold W. Brun
Executive Secretary
Minnesota State Medical Association



HEW Secretary, Elliot L. Richardson, was a featured speaker at the recognition dinner given Congressman Ancher Nelsen by the Minnesota State Medical Association and other health related organizations. Seated to the right of Secretary Richardson is Mrs. French, wife of Doctor Lyle French, Vice President for Health Sciences, University of Minnesota, who served as Dinner Chairman.



Representative Ancher Nelsen (center), Minnesota's Second District Congressman, is pictured here with MSMA President, Doctor George Martin (left) and MSMA President-elect, Doctor John J. Regan (right), during the social hour preceding the testimonial dinner given Congressman Nelsen on behalf of the Minnesota health science professionals.



Doctor Lyle French (right), Vice President for Health Sciences, University of Minnesota, is shown presenting a special appreciation plaque from the health science professionals to Congressman Ancher Nelsen. Also receiving a special recognition plaque from Doctor French was Congressman Paul G. Rogers (D), Florida, Chairman of the House Public Health and Environment Subcommittee, who spoke at the dinner.

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St. Mary's Physician Receives Award

Dr. John Warren, Golden Valley, was named recipient of the first annual Leonard A. Lang Obstetrics and Gynecology Teaching Award. The citation and cash award is given for excellence in teaching obstetrics and gynecology to a practicing physician who is a member of the clinical faculty of the University of Minnesota Ob Gyn Department. Dr. Warren is a member of that faculty, and teaches residents assigned by the University to St. Mary's Hospital for clinical experience in Ob Gyn.

The award is sponsored jointly by the Department of Ob Gyn at the University of Minnesota and by St. Mary's Hospital and was established in honor of Leonard A. Lang, M.D. clinical professor emeritus at the University of Minnesota and chief emeritus of the Ob Gyn service at St. Mary's.

Upstate Minnesota Physician Appointed Associated Editor of Modern Medicine

Dr. Stephen L. Zuckerman, a Diplomate of the American Board of Internal Medicine and a resident of Onamia, Minnesota, has been appointed an associate editor of MODERN MEDICINE.

Dr. Zuckerman is co-ordinator of health sciences education for the Tri-Hospital Association, consisting of St. Joseph's Hospital, Brainerd; St. Gabriel's Hospital, Little Falls, and Community Mercy Hospital, Onamia. He serves as consulting internist to all three institutions, and is a clinical assistant professor of medicine at the University of Minnesota.

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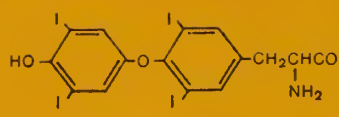
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Sodium Levothyroxine

Pharmacology: SYNTHROID (sodium levothyroxine) acts, as does endogenous thyroxine, to stimulate metabolism, growth, development and differentiation of tissues. It increases the rate of energy exchange, and increases the maturation rate of the epiphyses. Sodium levothyroxine is absorbed rapidly from the gastrointestinal tract after oral administration; following absorption, the compound becomes bound to the serum alpha globulin fraction. Accurate determination of either the PBI (protein-bound-iodine) or other appropriate tests may serve as a useful index of therapeutic response to SYNTHROID (sodium levothyroxine) therapy because of its affinity for serum proteins. The mean half-time of levothyroxine turnover is reported to be 6.5 days as measured by disappearance of radio-iodine (I^{131}) labeled levothyroxine from the serum in euthyroid subjects.

Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or anti-thyroid drugs. Indications for SYNTHROID (sodium levothyroxine) Tablets include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (non-toxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) for Injection is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdosage of SYNTHROID (sodium levothyroxine) may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting, and continued weight loss. While these effects may begin after four to five days, they may not become apparent for one to three weeks. Patients receiving the drug should therefore be kept under close observation for signs of thyrotoxicosis. If indications of overdosage appear, the medication should be discontinued for two to six days and then resumed at a lower level. Signs of optimal thyroid function will establish the proper maintenance dose.

The severity of diabetes may be reduced by hypothyroidism, and the requirement for insulin is often lowered. Therefore, patients with diabetes mellitus should be observed closely for possible changes in insulin or other antidiabetic drug dosage requirements.

If hypothyroidism is accompanied by adrenal insufficiency, such as Addison's disease (chronic adrenocortical insufficiency), Simmond's disease (panhypopituitarism), or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The patient's progress during thyroid treatment must be observed carefully and regularly for evidence of the development of any of these conditions.

Caution must be exercised in the administration of this drug to patients with cardiovascular disease; development of chest pains or other aggravation of the cardiovascular disease requires a reduction of dosage.

Contraindications: SYNTHROID (sodium levothyroxine) therapy is contraindicated in thyrotoxicosis and acute myocardial infarction.

Side effects: The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism: sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

In most cases with side effects, a reduction in dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and administration: The importance of careful diagnosis of hypothyroidism must always be considered, despite the fact that symptomatically the condition is one of the most clear-cut of endocrine disorders. Diagnosis should include laboratory testing of basal metabolic rate, serum PBI, and other tests for thyroid function to support clinical signs of thyroid hypofunction.

Treatment of hypothyroidism requires replacement of thyroid hormone in daily amounts adequate for maintaining normal metabolism. Reliable laboratory measurements and good clinical judgment will determine the daily dose required to achieve the goal of therapy. The correct concentration of thyroxine is essential for the health of all tissues; overdosage may lead to thyrotoxicosis medicamentosa, while underdosage permits the continuation of the hormonal deficiency.

Treatment can be guided by the serum PBI level (the normal range in males 4.5 to 7.5 mcg%; in females, 5.5 to 8.5 mcg%) produced after a few weeks the daily dose of thyroxine administered. A PBI level below 5 mcg% may indic the need for a larger dose of thyroxine. PBI levels are not absolute ind cators the thyroid state, however. In patients made euthyroid with SYNTHROID (sodi levothyroxine), it is not unusual to find PBI levels of 8 to 10 mcg% Levothyrox has a high binding capacity for serum proteins in contrast to other thyroid me caments which may contain varying amounts of L-triiodothyronine which ha low binding capacity.

In adult myxedema (when the PBI is often as low as 2.5 mcg% or less), starting dose of SYNTHROID (sodium levothyroxine) should be 0.025 mg da increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second weeks. A serum PBI, ECG, and clinical examination should be made after 30 d on this dosage regimen. In the event of an over-all rapid recovery the 0.1 daily dose should be continued, and the clinical status reviewed after an ac tional 30 days (total treatment period of approximately 90 days). The daily d may then be increased to 0.2 mg. After an additional two months on this regim clinical and PBI evaluations should be repeated. If either appears to be bel normal, the daily dose should be increased to 0.3 mg. Permanent ma intenar doses vary with the individual patient, ranging from 0.1 to 1.0 mg. da ly.

The same starting dose of SYNTHROID (sodium levothyroxine) as adm n ste for adult myxedema may be employed for cretinism or severe hypothyroid sm children, but all intervals of change should be made every two weeks. In growing child, final dosage requirements may be greater than in the adult. cases where cretinism is discovered after the first six weeks of life, overdos of SYNTHROID (sodium levothyroxine) therapy is much preferred to under-tre ment, in order to accelerate growth rate. As with the adult patient, serum may be measured during SYNTHROID (sodium levothyroxine) administration.

In hypothyroidism without myxedema (where the PBI usually ranges from to 4.5 mcg%), the starting dose of SYNTHROID (sodium levothyroxine) may 0.1 mg. daily and may be increased by 0.1 mg. every 30 days. Clinical eval at should be made monthly and PBI measurements about every 90 days. Final ma tenance dosage will usually range from 0.2 to 0.4 mg. daily, although h gl maintenance dosages are sometimes necessary.

In myxedematous stupor or coma, with no evidence of severe heart d sea 200 to 400 mcg. of SYNTHROID (sodium levothyroxine) for Injection may administered intravenously utilizing a solution containing 100 mcg per Detectable effects are usually observed by the sixth hour after injection and fully appreciated during the following day. A repeat injection of 100 to 200 m may be given on the second day if significant improvement has not occ r The intravenous use of sodium levothyroxine in myxedematous coma is edva tageous because it produces a predictable increase in the concentration protein-bound iodine, eliminates the need for multiple doses until oral thera is reinstated, circumvents the uncertainty of oral or intramuscular absorpti and avoids the risk of pulmonary aspiration. SYNTHROID (sodium levothyrox for injection is given by the intramuscular route when the oral route is impra cal and a rapid onset of effect is not desired.

It should be noted that in some patients whose PBI is 4.0 mcg% or e endogenous secretion is reduced when exogenous thyroid hormone is adm n tered. In these patients, the PBI does not increase as would be expected af a few weeks of medication. This may indicate the need for a longer period observation to ascertain the required dosage. In such patients, several mont may be needed to determine the correct maintenance dosage.

How supplied: SYNTHROID (sodium levothyroxine) Tablets are supplied scored, color-coded compressed tablets in seven concentrations 0.025 m (orange), 0.05 mg. (white), 0.1 mg. (yellow), 0.15 mg. (violet), 0.2 mg. (pin 0.3 mg. (green), and 0.5 mg. (blue).

SYNTHROID (sodium levothyroxine) for Injection is supplied in 10 ml. vi containing 500 mcg. of lyophilized active ingredient and 10 mg. of Mannitol N. a 5 ml. vial containing Sodium Chloride Injection, U.S.P., is provided as diluen

Directions for reconstitution: Reconstitute the lyophilized sodium levothyroxi by aseptically adding 5 ml. of the Sodium Chloride Injection, U.S.P., to the vi Shake vial to insure complete mixing.

Use immediately after reconstitution. Discard any unused portion.

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Psychiatry

Hysterical Neurosis

Conversion Type

ABRAHAM FLEMENBAUM, M.D.

Conversion hysteria is of clinical interest because of its striking and dramatic manifestations. There has been lack of agreement concerning definition of terms and the criteria for diagnosis; however, in its "classical" form it is a disorder diagnosed in the presence of the following characteristics: The patient is generally a young adult, usually female, with fixation in an early stage of psychosexual development, frequently with a premorbid personality of the "hysterical" kind. These patients, in the presence of a precipitating stress, usually of a sexual nature, "convert" their anxiety into somatic symptoms symbolizing psychological conflict.

Because anxiety is "converted" the patient presents *belle indifference* and this avoidance of anxiety by symbolization provides a very important primary gain. By obtaining attention, care, love, etc., from the family, the hospital personnel, and others, the patient receives also a secondary gain. The symptoms are usually expressed in the voluntary sensori-motor nervous systems, and therefore, originally were thought to be completely different from the psychophysiological reactions which were supposed to be expressed only in the "autonomic" nervous system.

As preferred defense mechanisms these patients use denial and repression.

Somewhat different clinical pictures, however, have evolved, probably related to the increased sophistication of medical knowledge of the patients.

Among these "newer" clinical pictures, some of which are well known and accepted, are the "compensation" neurosis, conversion symptoms "simulating physical illness," and symptoms "complicating physical illness."

There are other discrepancies in the "classical" picture. They stem from observations that patients with conversion hysteria frequently had fixations and personalities other than hysterical. They also stem from the fact that in some patients the symptoms were not clearly voluntary sensori-motor (i.e. nausea, vomiting, abdominal pain, etc.). It has also been found that under hypnosis and other conditions some autonomic functions can be affected. The cleavage between autonomic and voluntary sensori-motor nervous systems then is not so clear. "Conversion hysteria" is not a single disease but a syndrome consisting of at least two different disorders, (not including "compensation neurosis," childhood hysteria, or hysteria "complicating a physical illness"). For lack of a better name these disorders are here called Type I or "classical" and Type II or "reaction formation".

Clinical Observations: Similarities and Differences

The American Psychiatric Association's *Diagnostic and Statistical Manual II* defines hysterical neurosis, conversion type (300.13) as one in which:

> "the special senses or voluntary nervous system are affected, causing such symptoms as blindness, deafness, anosmia, anaesthesias, paraesthesias, paralyses, ataxias, akinesias, and dyskinesias. Often the patient shows an inappropriate lack of concern or belle indifference about these symptoms, which may actually provide secondary gains by winning him sympathy or relieving him of unpleasant responsibilities. This type of hysterical neurosis must be distinguished from psychophysiologic disorders, which are mediated by the autonomic nervous system; from malingering, which is done consciously; and from neurologic lesions, which cause anatomically circumscribed symptoms."[1]

Reports of clinical observations and erratic results obtained with treatment made it obvious that this picture of "classical" hysteria is not satisfactory for most cases of "hysteria". Clinical findings have shown that patients with these types of symptoms may later regress to full blown schizophrenia; this has been well known and has been frequently reported.[3,9,10,17,18,20,21]

Dr. Flemenbaum is a Research Fellow at the Adult Inpatient and Clinical Psychopharmachology Services, Department of Psychiatry, University of Minnesota, Minneapolis.

This report is a modified version of a paper which received an honorable mention in the William C. Menninger Award of 1970, when Dr. Flemenbaum was Senior Resident.

An intriguing fact is the extraordinarily consistent choice of inadequate and frequently abusive husbands. These husbands also show a high incidence of alcoholism and other sociopathy. Both of these facts have been reported by Blinder[2] and Slater.[17] It has also been reported recently by Guze that among relatives of convicted criminals there is an increase of conversion hysteria.[7]

A more sophisticated society does not tolerate "classical" hysteria. There is a decrease in it, but with compensatory increase of pictures characterized by pain, usually in the abdomen or head, and disorders "simulating physical illness".[21] This has changed either the picture of classical clinical conversion or its frequency to such a point that now many patients are referred to psychiatry only after expensive and extensive medical and neurological work-ups, after multiple hospitalizations, often when the patient has had innumerable operations (and abdomens that have been called "battle ground or checker board abdomen"), or is "hooked" on pain medication. The "classical" picture of conversion is infrequently seen now and almost exclusively is related to extreme environmental deprivation, rigid religious education, related to mental retardation, or as symptoms of an incipient schizophrenia.

Several authors tend to consider hysteria conversion as more of a syndrome than a specific disease entity for these reasons: multiple ethiology; neurosis, schizophrenia, endogenous depression; variety of clinical pictures; "classical vs. preschizophrenic vs. polisymptomatic.[12,13,17]

Even with all the differences in clinical manifestations of patients with the "syndrome", most articles and textbooks still recommend making the diagnosis on the basis of positive findings and not only when physical disorder has been ruled out. These positive findings include: a history of symptoms (past or concurrent) that clearly appear conversive, such as paralysis and anesthesias; other psychoneurotic symptoms such as anxiety, depression, obsession phobias; a past history of multiple illness or multiple surgery with no clear cut physical origin; a history of sex disturbances with frigidity and/or distaste for sexuality; behavior manifestations of hysterical personality; the presence of *belle indifference;* a history of recent death of a person important to the patient or similar disturbances in personal relatives temporarily related to the onset of the symptoms.[11]

As can be seen here, even though these diagnostic characteristics of the disorder include "modified" ones, they are still "classical" in that the patient has to have some hysterical personality characteristics or other classical symptoms of conversion (*belle indifference,* neurotic symptoms frigidity and/or distaste for sex, etc.).

The other side of the coin in the problem of definition of hysteria is represented by Robbins, Perley, and Guze. These authors developed a definition of the clinical picture of hysteria after the findings of Purtell, et al.,[13] of a "characteristic clinical picture of women with a diagnosis of hysteria" in which (a) they had at onset an age of less that 35 years; (b) the disorder was seen rarely or not at all in men; (c) it was never monosymptomatic (minimum of 11 symptoms per patient); (d) vague, unclear complaints; (e) a history of excessive hospitalizations and surgery, (f) and sexual frigidity and/or dysmenorrhea, dyspareunia, etc.

With these findings Robbins and O'Neal suggested specific clinical criteria,[16] that, slightly modified by Perley and Guze[12] and then again modified by Guze, et al.,[5,6,7] are presented as follows:

1. The patient has to present a dramatic or complicated medical history before age 35.
2. The patient has to report at least 25 of the following symptoms, in at least nine of the ten groups of symptoms:

   Group 1: feeling sick most of one's life, headache
   Group 2: blindness, paralysis, anaesthesia, aphonia, fits of convulsions, unconsciousness, amensia, deafness, hallucinations (in the absence of psychosis) or urinary retention;
   Group 3: fatigue, lumps in the throat, fainting spells, visual blurring, weakness, dysuria
   Group 4: breathing difficulty, palpitation, anxiety attacks, chest pain, dizziness;
   Group 5: anorexia, weight loss, marked fluctuation in weight, nausea, abdominal bloating, food intolerances, diarrhea or constipation;
   Group 6: abdominal pain or vomiting;
   Group 7: dysmenorrhea, menstrual irregularity including amenorrhea of at least two months excessive menstrual bleeding;
   Group 8: sex indifference or frigidity, dyspareunia or other sex difficulties, hospitalization for hyperhemesis gradivarum or vomiting for all nine months of pregnancy;
   Group 9: back pain, joint pain, extremity pain burning pains of the sex organs, or of the rectum, other bodily pains;
   Group 10: nervousness, fears, depressed feelings

quitting work, inability to carry regular duties, easy crying, hopeless feelings, thinking of suicide and suicide attempts.

All these authors maintain, that not only course nd outcome but also diagnosis are highly unreliible, when using previous definitions contrasting /ith high (90% and higher) reliability of diagnois (and outcome) of hysteria when made with ieir own criteria.

At the University of Minnesota Hospitals, about 0 to 40 percent of the consultations are for "hysria" of a type similar to the patient described by uze, et al. but there are, however some differnces. These differences and similarities are as ollows: The patient is usually a middle aged emale. She has had a 15 to 20 year history of ain with a history of multiple operations and 10 o 20 hospitalizations with very extensive workips. She does *not* show *belle indifference;* on the ontrary, she has complained a great deal for many ears and has manipulated her family and her hysicians so well that she is already, or nearly, rug addicted. (See Table.)

These patients may also have hysteroid prenorbid personalities. Frequently "oral" dependncy is marked, but the patient has used reactionormation extensively, permitting her to appear a ard worker, reliable, and a self-sufficient individal. This continues until the symptoms become so intense, and pain so constant" that she "had o quit working" and stopped taking care of her esponsibilities.

Aside from the satisfaction of oral dependency eeds, no other primary unconscious conflict that ad to be symbolically "converted" can be found; herefore, in this type of patient, primary gain, f existent at all, is completely unimportant. The ttention, care, and love of the family, the hospital personnel, the physician, or the welfare worker, coupled with relief from unpleasant and/or unwanted responsibilities, make the so called secondary gain of the "classical" type become all important, to such a point that we can say that *the secondary gain becomes the primary gain* and vice versa.

Another difference in this type of patient when compared with the classical ones is that it is frequently impossible to find in the anamnesis any specific precipitating stress aside from the finding that responsibilities become too large (or the family stops paying attention to the patient for one reason or another) just before her symptoms flare up. For this reason we can say that another clear difference between these two types of hysteria conversion is in the area of conflict resolution. On the one hand, in the classical type, under stress the unconscious drives are converted by symbolization into physical signs. In the second type a hard working, independent patient, in no acute conflict, can, without losing face, abandon his/her responsibilities and get fulfillment of his/her dependency needs by somatization. This somatization is usually reinforced by the father or the husband who somehow obtains some gain with it.

Examples include a busy stock man who comes home several times during the day due to multiple complaints by his wife. In another case, an elderly husband, who had been ordered to rest after myocardial infarction was not only working in his job but would cook and do all the house chores for his wife was "incapacitated" by multiple pains.

Slater[17] also found some evidence of reinforcement of the somatic symptoms by members of the immediate family (which he was tempted to call a *"follie a deux"*). He noticed four cases in which at least one family figure, the father or the husband, was busily employed fostering the illness.

These patients often have family histories simultaneous in two extremes: some members of the family are either alcoholic or delinquents; others are "pillars of the community". They are the "all-American family" people, hard workers, PTA goers, taxpayers, "law and order" people, football players, which suggests the possibility of reaction formation again.

Another common observation in the psychiatric interview is a family history that is positive for somatization. "Imitation and identification", especially with significant members of the family, has been frequently reported.[11,17,21]

The somatization of these patients can simulate practically any medical disorder. Sydenham observed that "hysteria imitates almost every disease that befalls mankind." Sometimes the symptoms are even "shaped" with time by consultation with different physicians. Symptom patterns change with changing medical knowledge on the part of the patient and with his aculturation and sophistication.[21] Symptoms start relatively early in life but they may not interfere with the activity that the patient really enjoys (in extreme cases they may skate but won't cook).

Other Evidence in the Literature

These findings are consistent with the literature

as mentioned above.

With regard to hysteroid personality, even in the "classical" type, many studies[2,4,9,21] emphasized that hysterical personality is not a condition "sinequa non" for the diagnosis of hysteria conversion. Slater, for example, found in his study that only about one-fourth of the cases had hysterical traits, but some showed sexual interests that were both late and feeble and failure to marry was found in many cases, which can be a sign of hysterical traits.[17]

Referring to precipitating stresses the literature appears confusing. On one hand, are reports like the one by Barham.[1] He states that in a follow up of 100 patients with hysteria "precipitating factors were present in every case even though in a few cases they were fairly difficult to elicit."

On the other hand, Slater[17] found that in about one-half of his cases there was nothing he could "put his finger on"; in some cases the stresses were "banal" and in very few, stresses "could hardly have been effective save for a pre-existing hysterical predisposition."

Slater[18] found that of the final group of patients originally diagnosed as "hysteria" in which no underlying physical pathology could be found (21 patients), the seven patients that had the "typical" (classical?) conversion syndrome all had definite psychogenesis (precipitating factors?) for their disorder. The patients that have definite precipitating factors (which grossly correspond more to a description of the "classical" type than to the nonclassical type or type 2) have a better prognosis.

In Barham's study, 66% were well at the time of the follow up. A total of 83% were still functioning four to six years after discharge, most, without any psychotherapy at all. Slater[18] found that the seven patients that had "typical" conversion syndrome were all well on follow up even though "three of them had shown some tendencies to develop symptoms when stressed" (which was also true for some patients in Barham's study).

This good prognosis on follow up contrasts sharply with that of the patients diagnosed using the stricter diagnostic criteria. Ninety percent or more of these patients had a poor prognosis. In Slater's follow up,[18] for example, he found of the 21 patients in which no underlying physical pathology could be found, there were 14 patients who resembled our type 2; five of these patients were partially disabled, three were totally disabled, and the rest were also considered chronic cases.

It is well accepted that hysterical symptoms can be found in a multiplicity of disorders including schizophrenia.[1,2,3,4,5,6,9,10,12,17,18,20,21] There is however, an alarming, and in some papers almost unbelievable high, frequency of neurologieal disorders (and even death) discovered in the follow up studies.[5,6,12,17,18,20]

Most of these studies were done following patients discharged from *neurological* hospitals. In the study with the worst results,[20] a 25 year follow up was conducted on patients discharged from the Boston Psychopathic Hospital. Out of 66 patients 22 had psychotic diagnoses and 14 patients had died of "organic" disorders. We observed though that the diagnosis of "hysteria" was so freely given that three cases with delusions or hallucinations on admission were still diagnosed as such.

That there are "clinically different 'hysterias'" has been previously noted. Ziegler,[21] for example concludes that there are "four different clinical types of conversion reaction: (a) "classical" with "loss of function" or "hysteroepilepsy"; (b) simulation of known organic entities; (c) those in which body pain is prominent; (d) conversion symptoms intermingled with those of an organic and/or psychophysiological nature.

These four types of hysteria can be summarized in our two types: the classical and the nonclassical.

Guze[5,6] also differentiates between what he calls "hysteria", following his rather strict "medical" diagnostic criteria, and "conversion symptoms."

These "conversion symptoms" are not only monosymptomatic but rather "classical" like: amnesia, paralysis, aphonia, blindness, anesthesia, etc., and he specifies that they are the so-called "pseudoneurological or grand hysterical symptoms" but probably because of anti-analytieal biases no other diagnostic criteria were used. They were referred to as unexplained symptoms suggesting neurological disease."

If diagnosis of "conversion" symptom was not given so freely and if the diagnostic criteria as summarized above (including psychoanalytical concepts of symbolization, primary and secondary gain, *belle indifference*, etc.) were used to make the diagnosis, many patients diagnosed in the follow up as schizophrenic personality disorders, neurological disorders, etc., would probably have been ruled out.

Summary

Two extremely different types of hysteria have been described in the literature; one "classical" using psychoanalytical concepts by the author and Guze et al. using only "medical" concepts. The author proposes a third type in middle ground using both psychoanalytical and medical concepts (probably includes Guze's type) and the diagnostic characteristics are summarized in the Table.

TABLE
Hysteria Conversion

Characteristic	Type I "Classical"	Type II "Reaction-Formation" Hysteria
Age	Adolescent-young adult	Usually middle aged
Sex	More frequently female	Almost always female
Premorbid Personality	Hysteroid?	Oral dependent
Psychosexual Dynamics	Oedipal fixation	Pre-genital fixation—Oral?
Environmental Precipitating Factors	Present - sexual?	Not present—satisfaction of dependency needs
Family History	Hysteria may or may not be present—family is usually religious, unsophisticated, from small towns, etc.	Hysteria frequently present—alcoholism and delinquency are frequent or the family is extremely conventional, rigid (a reaction formation?)
Conflict Resolution	By symbolization "conversion"	Satisfaction of dependency needs—relief from responsibilities
Most Used Defense Mechanism	Denial—repression	Reaction-formation?
Primary Gain	Most important	Minimal—may not be present
Secondary Gain	Secondary	Becomes the primary (most important)
Belle Indifference	Present "obvious clinically"	Not present or weak "You have to search for it"
Symptom Expressed Through . . .	Voluntary sensori-motor plus nausea, vomiting hiccups, etc.	Abdominal pain, back ache, headache, bizarre disease picture
Frigidity	Present	May be totally absent
Number of Symptoms	Monosymptomatic	Multiple
Complaint	Localized, precise	Vague, multiple
Polisurgery Polihospitalization	Not present	Present
Response to "Suggestion"	Fair to very good	Very poor

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Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose® packages of 1000.

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(diazepam)

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If you wrote a prescription for 100% allergen-free air, we'd come within 1% of filling it. We're the ultra-clean air people. We're Dexon, Inc. — makers of Prime-Aire® Purifiers.*

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Two portable models are available. The illustrated Prime-Aire console model purifies the air in an average 1200 square foot home at least once an hour. This model is 18″ x 18″ x 22″ high and weighs 35 lbs.

Our table model (not shown) filters the air in a 12′ x 12′ room five times an hour. It is 18″ wide by 14″ deep by 9″ high, and weighs only 18 lbs. Both models are UL listed.

Easy care

The HEPA filter needs no washing. It's replaced about once a year if used continually. And less often if used seasonally. The pre-filter is replaced monthly during continuous use.

Ordinary purifiers can't compare

Prime-Aire must not be confused with electrostatic devices. The Dexon HEPA filter never needs cleaning. Electrostatic filters require frequent removal and washing. Prime-Aire's filtering efficiency is rated at 99% and beyond. Average reported efficiency of electrostatic devices is 85%. Prime-Aire provides whisper-quiet operation. There's no arcing, snapping or ozone gas as generated by electrostatic methods.

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With Prime-Aire, many allergy patients have a proven weapon to fight — and often prevent — their suffering and discomfort. When breathing Dexon's ultra-clean air, many of these people report a degree of relief they never before thought possible.

An aid in many places

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Medical data

To obtain documented performance data, write: Dr. I. A. Ismail, Director of Medical Products, Dexon, Inc., 3440 Belt Line Blvd., Minneapolis, Minn. 55416. Phone: (612) 927-5671

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The Advertising Pays for Your Journal



rheumatoid arthritic blowup...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, adding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.

Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.

Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.

Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.

Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.

Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.

(B)98-146-800-E

For complete details, including dosage, please see full prescribing information.

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TA.8356-9



a new outlook in chronic pain

of moderate to severe intensity

Though Talwin® Tablets, brand of pentazocine (as hydrochloride), can be compared to codeine in analgesic efficacy, Talwin is not subject to narcotic controls. Patients receiving Talwin Tablets for prolonged periods face fewer of the consequences you've come to expect with meperidine or codeine. And that, in the long run, can mean a better outlook for your chronic-pain patient.

Talwin Tablets are:

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- **Not subject to narcotic controls:** convenient to prescribe – day or night – even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See last page of this advertisement for a complete discussion of adverse reactions and a brief discussion of other Prescribing Information.)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few patients in association with the use of Talwin although no causal effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition. *Treatment.* Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

Winthrop Winthrop Laboratories, New York, N. Y. 10016 (15

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

President's Letter



Growth

To be aware of Minnesota's changing health profession education is exciting and awesome. It reflects the increasing awareness on the part of medicine and lay groups, that cooperative endeavor is needed to solve our health care problems.

To become a physician one must learn to solve a problem by diagnosis, prognosis and then management. In Minnesota today medical educators, physicians, legislators, governing boards of educational and health institutions are struggling to learn these same skills and mastering them with evident progress and further plans to improve health care for our State and its neighbors. The development of the University of Minnesota Health Sciences as an integral unit is one example. The new University curricula and the establishment of the Duluth Branch School of Medicine are other examples. This issue of Minnesota Medicine is dedicated to the new Mayo School of Medicine and it's first class of 40 students. That event is the result of arduous labor by many dedicated people. Dr. Emmerson Ward, Chairman of the Mayo Board of Governors, Dr. Raymond Pruitt, Dean of the Mayo Medical School, and their staffs, as well as the Mayo Foundation, deserve not only our congratulations but active support.

There has never been a time when the practicing physician and the health educator are as important to each other. From acceptance to medical school 'til cessation of all medical activity, each physician is student, practitioner, teacher. To disavow part of this continuum jeopardizes our ability to diagnose, prognose, and manage an individual's health problems or society's health problems.

I am confident that Minnesota physicians join with me in applause for what is being done and active support for continuing exploration of what is yet to be done.

George B. Grantin

President
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Pulmonary Vasculitides

Importance of the Clinical and Pathologic Differentiation

RICHARD A. ARMS, M.D., DAVID E. DINES, M.D. AND RICHARD A. DeREMEE, M.D.

Several classifications of the vasculitides have been described in the literature.[1-3] Some authors[4,5] have postulated that the necrotizing vasculitides represent a continuum of tissue changes ranging from pure necrosis and granuloma formation to pure angiitis. The diseases that should be considered as pulmonary vasculitides include Churg-Strauss vasculitis, periarteritis nodosa, allergic angiitis, Wegener's granulomatosis, and the pulmonary infiltration with eosinophilia (P.I.E.) syndromes. The pulmonary vasculitides have been classified pathologically by Alarcón-Segovia and Brown.[6] The clinical classification that we have found workable is shown in the Table.*

Goodpasture's syndrome (lung purpura and nephritis) is a pulmonary-renal syndrome usually occurring in young males, commonly with a fulminating and fatal outcome.[7] Recent evidence has suggested that an auto-immune mechanism is operative,[8] but Goodpasture's syndrome and idiopathic pulmonary hemosiderosis are not included in a classification of pulmonary vasculitis because, pathologically, they do not show true vasculitis.[9]

By considering both the clinical and the pathologic features, one can usually make an accurate diagnosis. However, the vasculitides should be differentiated among themselves because the prognosis is different for each and because corticosteroids and immunosuppressive agents may be of value for the treatment of some.

Churg-Strauss Vasculitis

Churg-Strauss vasculitis, also called angiitis granulomatosis, was first described in a retrospective study in 1951.[10] All 13 patients in the study had a syndrome characterized by asthma, marked eosinophilia (eosinophils as high as 84%), and extravascular granuloma formation. Eleven of the 13 patients had died at the time of the study, the chief cause of death being heart failure secondary to myocardial damage and intracerebral bleeding. Typically, the asthma abated and often completely disappeared during the course of the terminal illness. Asthma preceded the terminal illness by an average of three years. Pulmonary involvement resembling Loeffler's pneumonia was noted on the chest roentgenograms in about 70% of patients.

Multisystem disease similar to periarteritis nodosa is characteristic of Churg-Strauss vasculitis and, on pathologic examination, nodular swellings along the course of small arteries can be seen grossly. All stages of necrotizing arteritis with invasion predominantly by eosinophils are usually found. The main difference from periarteritis the presence of the characteristic extravascular granulomatous nodules. Similar nodules have been observed in the lungs of patients with Loeffler's syndrome and Wegener's granulomatosis. In Churg-Strauss vasculitis, these lesions are seen in the lung parenchyma of half of the patients, and in the pulmonary arteries of about 70%.

Since the original description of this entity, very few cases have been published. Inclusion of this disease in other categories of vasculitis partially accounts for its apparent low incidence. A recent case of Churg-Strauss vasculitis is herein presented to describe the clinical and histologic factors that help differentiate it from the other pulmonary vasculitides.

Case Report

A 55-year-old man was seen initially at the Mayo Clinic in 1967 for evaluation of bronchial asthma. He had a three-year history of symptoms compatible with typical nonseasonal asthma of progressing severity. Of significance was a past history of vasomotor rhinitis, nasal polyps, and multiple allergies.

Physical examination revealed no abnormalities except for inspiratory and expiratory wheezing and a prolonged expiratory phase. The chest roentgenogram was normal. Pulmonary function studies showed airway obstruction

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

*See page 874.

with good reversibility after the use of nebulized isoproterenol. Results of all other laboratory studies were normal except for 8% eosinophils. The patient was instructed to reduce the dose of cortisone that he had been taking and to continue with hyposensitization and various bronchodilators.

The patient returned in November 1971 for re-evaluation. He had had no further bronchospasm since the previous summer. However, a spasmodic cough with occasional hemoptysis had developed. During this time, he also had developed recurrent asymptomatic skin lesions resembling "blisters"; these were especially severe on the tongue, lips, and hands. Physical examination showed a small ulcerating lesion of the hard palate and vesicular lesions of the hands and arms. The lungs were clear and were without evidence of bronchospasm. Laboratory studies included a leukocyte count of 34,600/cu mm. with 85.5% eosinophils. Urinalysis showed hematuria of grade 2; creatinine clearance was 80 ml/min. The chest roentgenogram revealed an ill-defined density in the left lower lobe. Results of pulmonary function tests were essentially normal, with only a slight decrease in the maximal midexpiratory flow rate. Bone marrow examination indicated severe marrow eosinophilia. Biopsy of one of the skin lesions revealed fibrinoid necrosis of vessel walls and an extravascular granulomatous reaction compatible with Churg-Strauss vasculitis.

Periarteritis Nodosa

Periarteritis nodosa was originally described in 1866 by Kussmaul and Maier,[11] and was considered to be rare until 1923, when Ophuls[12] described the second case—one with pulmonary artery involvement. He enumerated nine features that differed from the original description; and after his publication, the term "periarteritis nodosa" included many vasculitides, making the incidence of pulmonary involvement with this entity difficult to ascertain. Rose and Spencer[13] reviewed 111 cases of periarteritis nodosa and found that 28% of the patients had pulmonary involvement; however, some of these may have had Wegener's granulomatosis, Churg-Strauss vasculitis, or allergic angiitis because the pulmonary vasculitides were not as well defined in 1957. The incidence of pulmonary involvement in pure periarteritis nodosa is probably less than 10%.

Periarteritis nodosa can occur at any age and affects males more often than females. It frequently presents as a multisystem disease, although selective involvement such as mononeuritis multiplex may be the only presenting feature. Typically, the disease has an intermittent course and is uniformly fatal in a few months to several years. Renal involvement is the most striking abnormality. In 52 of 66 patients studied by Rose and Spencer,[13] hematuria and early renal failure occurred. Hypertension often occurs late in t disease. The pulmonary involvement that is se probably occurs more frequently in the bronch arteries. The findings on the chest roentgenogra are nonspecific and consist primarily of patc parenchymal infiltration; pleural and pericard effusion as well as infarction with cavitation c be seen occasionally.

On pathologic examination, the lesions a often visible grossly and occur in small a medium-sized muscular arteries, particularly their bifurcations. Microscopically, focal lesio in several stages of development are characterist the initial manifestation being fibrinoid necro with infiltration of polymorphonuclear leukocyt Eosinophilia is not necessary for the diagnos and giant cells and granulomas are usually n seen.

Allergic Angiitis

Allergic angiitis is typically an acute vascul reaction largely attributed to exposure to scru or drugs, resembling the Arthus type of reaction Clinically, either the course is fulminating and u remitting or the patient recovers without recu rence once the offending agent has been remove Cutaneous involvement is prominent and syn metric, particularly in the dependent portions the body. The lungs are frequently affected, a the chest roentgenogram may show nonspecif features similar to those seen in periarteriti Chronic renal disease, hypertension, and peripl eral neuropathy are usually not part of the fin ings of allergic angiitis.

Pathologically, only small arteries and veins a affected. In contrast to periarteritis nodosa, a lesions appear to be at the same stage of inflan mation; there is no predilection for bifurcations aneurysmal formation. The vessels show an i tense cellular response, with prominence of eosin phils.

Wegener's Granulomatosis

Three related entities can be categorized Wegener's granulomatosis: (1) Wegener's granul matosis with renal disease, (2) limited Wegener granulomatosis and (3) midline granuloma.

Wegener's granulomatosis is classically con posed of the triad of necrotizing granulomas the upper respiratory tract, disseminated angiiti and focal glomerulitis. In most series, two thir of the patients have destructive granulomas of th upper respiratory tract, and an even greater pe

ntage have pulmonary infiltration. Clinically, e disease is characterized by a severe and pro- essive sinusitis, cough, and finally, in most ses, renal failure.[15,16] On microscopic examina- n,[17] arteritis and phlebitis are generally separate m the areas of necrosis. This can be difficult prove, however, because necrosis may destroy e evidence of vasculitis. Treatment of Wegen- 's granulomatosis with immunosuppressive ugs (azathioprine, 150 mg/24 hr, or chloram- cil, 2.0 mg/24 hr) has brought about a 1-year rvival rate of 80% as compared to 34% with roids and 18% for patients who are not treat- l.[18] In one series, cyclophosphamide, in a dose 50 to 125 mg/24 hr, has resulted in a partial or mplete remission in seven of nine patients with Vegener's granulomatosis.[19]

Lethal midline granuloma is an invariably fatal lness characterized by progressive destruction of e facial structures by an inflammatory process. lthough granulomatosis accompanies the necro- s, true vasculitis does not occur. This entity, owever, should be included within the classifica- on of disorders under discussion.

Recently, a limited form of Wegener's granu- matosis has been described in which only the ungs apparently are involved. Carrington and Liebow[20] have described 16 patients who had the linical features and pulmonary lesions identical o those of Wegener's granulomatosis, but without he characteristic renal involvement. The chest oentgenogram in the limited form shows multiple, ilateral, frequently cavitating, thin-walled lesions rimarily in the lower lung fields,[21] which clini- ally may simulate neoplasm or infectious caseous granuloma. For the diagnosis of limited Wegener's granulomatosis, there must be microscopic evi- dence of vasculitis and separate necrotizing granulomas in the pulmonary biopsy specimen. There is no specific pattern of response to therapy, but there may be longer survival in the limited form.

Case Report

A 74-year-old white woman presented with the chief complaint of shortness of breath. Approximately four months before admission, she noted a gradual onset of dyspnea on exertion and easy fatigability. This was subsequently accompanied by a loss of 18 pounds in spite of a good appetite and apparently adequate food intake. She was hospitalized, where she was treated for congestive heart failure and depression with digitalis and Triavil, a tranquilizer-antidepressant, with little or no change in her status. Shortly before referral to the Mayo Clinic, a chest roentgenogram revealed multiple bilateral ill-defined nodular lesions suggestive of metastatic carcinoma.

On physical examination, the temperature and pulse were normal. The blood pressure was 170/106 mm Hg. She appeared pale and chronically ill. A few scattered nonspecific basilar rales were heard on auscultation of the chest. There was a grade 2/6 ejection systolic murmur heard best in the aortic area and transmitted along the left sternal border. There were no gallops and the jugular venous pressure was normal.

Results of urinalysis and routine blood counts were normal. The serum creatinine level was 0.85 mg/100 ml, and the 12-hour creatinine clearance was 78 mm/min/1.73 sq m. An induced sputum for malignant cells was negative. Sputum cultures and serologic tests for fungi also were negative.

A chest roentgenogram four weeks later showed that some areas had improved and others had worsened. Because of this changed pattern, the diagnosis of vasculitis was considered and open-lung biopsy was undertaken. The open-lung biopsy revealed a necrotizing granulomatous lesion consistent with the localized form of Wegener's granulomatosis.

Therapy with cyclophosphamide, 50 mg twice a day, was started. Approximately two weeks after therapy was begun, the patient noted an increased sense of well-being and a chest roentgenogram revealed improvement.

Pulmonary Infiltration with Eosinophilia Syndromes (P.I.E.)

Loeffler's syndrome[22,23] is a typically benign condition characterized by eosinophilia and migrating lung infiltrates that may be unilateral or bilateral and located in any part of the lung. Clincially, the symptoms may include mild to high fever, severe bronchospasm, and shortness of breath. The percentage of eosinophils in the blood may range from 10% to 80%. In only a few cases of Loeffler's syndrome has biopsy been done; the usual finding is interstitial and alveolar edema with eosinophil infiltration.

Carrington and co-workers[24] have described nine patients with chronic eosinophilic pneumonitis who had a chronic life-threatening illness with high fever, night sweats, loss of weight, and severe dyspnea. Most patients had tuberculosis as the initial diagnosis. Six patients had asthma. The roentgenogram of the chest showed characteristic rapidly progressive dense infiltrates. Lung biopsies showed chronic interstitial pneumonitis with fibrosis. Corticosteroid therapy resulted in complete clinical recovery and roentgenographic clearing in five days.

Because Loeffler's pneumonia has terminated in fatal periarteritis nodosa,[25] Loeffler's syndrome

and chronic eosinophilic pneumonitis must not be considered invariably benign disorders but rather a spectrum of a disorder in the vasculitides classification.

In Loeffler's syndrome, treatment can be based on the acuteness and severity of the illness; not all patients with Loeffler's syndrome need to be treated. The acutely ill patient with Loeffler's syndrome and the patient with chronic eosinophilic pneumonitis presenting with fever, loss of weight, night sweats, and dyspnea should be treated with corticosteroids—prednisone, 40 mg/day or 60 mg every other day. The dose should be tapered to a maintenance dose or be discontinued, depending on the clinical response. All patients with positive tuberculin test reactions should be treated prophylactically with isoniazid, 300 mg/day, while on the corticosteroid regimen.

TABLE
Clinical Classification of the Pulmonary Vasculitide

- **Churg-Strauss vasculitis**
- **Periarteritis nodosa**
- **Allergic angiitis**
- **Wegener's granulomatosis**
  - **Wegener's granulomatosis with renal involvement**
  - **Limited Wegener's granulomatosis**
  - **Midline granuloma**
- **P.I.E. (pulmonary infiltration with eosinophilia) syndromes**
  - **Loeffler's syndrome**
  - **Chronic eosinophilic pneumonitis**

Conclusions

The pulmonary vasculitides include a wi range of disorders. By considering both the clin cal and the pathologic features one can usual make the diagnosis. The disorders must be di tinguished among themselves because the progn sis is different and because corticosteroids an immunosuppressive agents may be of value i the treatment.

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But as in cutting up a man that's dead,
The body will not last out, to have read
On very part, and therefore men direct
Their speech to parts, that are of most effect;
So the worlds carcasse would not last, if I
Were punctuall in this Anatomy;
Nor smels it well to hearers, if one tell
Them their disease, who faine would think they're well.*

*John Donne: An Anatomie of the World, The First Anniversary. Lines 435-442 1611.

Surgical Treatment of Thyroid Nodules

OLIVER H. BEAHRS, M.D. AND CLARENCE R. PETRIE, M.B., Ch.B.

Nodular goiter occurs frequently and is cognized in possibly as high as 50% of the ases. In a recent study of approximately 150,000 atients at the Mayo Clinic (200,000 effective egistrations), 3,000 patients were seen who were oted to have significant goiters of various types. ome patients were observed only; some received edical treatment (radioactive iodine, usually for xophthalmic goiter, thyroid replacement therapy or Hashimoto's thyroiditis, and symptomatic reatment for subacute thyroiditis), and the remainder were treated surgically. Thyroidectomy vas performed on 365 patients. Of the operations erformed, 347 were for nodular goiter: 14 for yperthyroidism, 18 for known cancer, and the thers for factors leading to an increased suspicion f cancer (or for other symptoms). Fifteen per- ent of the nodular goiters proved to be carcinoma.

It is neither practical nor feasible to resect all linically apparent nodular goiters. Selection for hyroidectomy must be made on the basis of the istory, the physical findings, and the laboratory nformation. Also the decision is based on the udgment of the physician regarding significant risk to the patient if the goiter is left untreated as opposed to the risk, inconvenience, and cost of removal. Indications for removal include the objectionable cosmetic appearance of obvious goiters, pressure symptoms or compression of other anatomic structures of the neck (trachea and esophagus) and thoracic inlet (including major vessels), hyperthyroidism or the risk of its development if the goiter is of considerable bulk (possibly 10% or more of nodular goiters), and, lastly, known or suspected underlying cancer. The decision to remove a nodular goiter for cosmetic appearance or pressure symptoms is easily reached. If there is no contraindication to surgery (cardiac, pulmonary, or other significant disease), thyroidectomy is the most immediately effective treatment for an adenomatous goiter with hyperthyroidism. The decision as to treatment of nodular goiters that are obviously cancerous is not difficult. Controversy and difference in selection of treatment result when a nodular goiter is present, when it is not suspected of being a cancer, and when the patient is asymptomatic. The decision is complicated further by the fact that there are some investigators who think that cancer of the thyroid gland either does not exist or is of such a "benign" nature that it does not require treatment; there are others who think that cancer of the thyroid should always be treated radically. Treatment lies between these extremes and the differing biological behavior of thyroid cancers must be recognized. At one extreme is the papillary adenocarcinoma, which is slow growing with the patient living many years before the lesion causes symptoms or death; at the other extreme is the anaplastic cancer, which grows rapidly and kills in a matter of months.

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Contributing Factors

Brief comments follow on the many factors that contribute to the judgment to remove a nodular goiter.

Age of Patient

The risk of cancer in a nodular goiter in a child is approximately 50%. In the adult, probably an incidence of 5 to 10% in surgically removed goiters is reasonable to expect. Our previously reported figures were 7.5% in all nodular goiters and 3.8% in asymptomatic nodular goiters not suspected of being cancer. More recently, the overall figure has been 12 to 14%.

Sex

Goiters are more frequent in women than in men. However, the incidence of cancer in nodular goiter is greater in men. On this basis, a man with a nodule in the thyroid gland is more often a candidate for thyroidectomy than is the opposite sex.

History

If a goiter has been present for many years without significant change in size, the risk of cancer is less than if the lesion is new or has recently shown an increase in size. Sudden enlargement and pain in a nodule are likely indications of hemorrhage into a pre-existing adenoma. Cancers are rarely painful. History of radiation exposure to the neck during childhood is significant in a patient with a recently noticed nodule in the thyroid in that it increases the risk of malignancy. Medullary cancer (Sipple's syndrome) is familial in many cases, and a history of thyroid cancer in family members must be given consideration.

Physical Findings

A discrete solitary lesion is considered more likely to be cancer than a multinodular goiter. "Single" is a term not used to describe nodules of the goiter because often what is considered to be a "single" nodule clinically proves to be a multinodular goiter on surgical removal. In a multinodular goiter, a discrete nodule within it might be a cancer or a cancer might co-exist without being evident on palpation. The consistency of the lesion is important; if it is firm but not hard like calcium, cancer is more likely than if the tumor is soft and cystic. However, a follicular cancer can be relatively soft. If fixation to overlying tissue is evident, cancer should be suspected, but it must be remembered that Riedel's struma and granulomatous thyroiditis might also be somewhat fixed to adjacent tissues. When cervical lymphadenopathy is present the thyroid gland should always be carefully palpated. In our experience 22% of papillary adenocarcinomas of the thyroid are first diagnosed by excision of an abnormal cervical lymph node. Venous congestion of the veins of the neck leads one to suspect pressure within the thoracic inlet, possibly by a goiter projecting into the chest.

Laboratory Findings

Laboratory function tests contribute little to the diagnosis of cancer except for the determination of thyrocalcitonin in suspected medullary adenocarcinoma. Levels above 800 picograms per milliliter (800 pg/ml) are diagnostic of the tumor even though no goiter can be palpated. In questionable hyperthyroidism, the results of thyroxine and radioactive iodine uptake studies are of value. In nodular goiters suspected of being Hashimoto's thyroiditis, thyroxine levels may b normal or high. For granulomatous thyroiditis th sedimentation rate is high (about 100 mm/hr The radioactive iodine scan will determine wheth the nodule takes up little or no iodine (col nodule), in which case cancer is more likely pre ent, or whether it takes up an increased amou (hot nodule), in which cancer is much less likel Findings on scanning are not absolute. In a grou of patients with cancer of the thyroid, 60% ha cold nodules; in 34% the scans were norma and in 6% the area of the nodule or the nodul itself was hot. Therefore, the result of the sca itself must not dictate the management of th goiter. X-ray examination of the chest will aid i determining whether there is deviation or com pression of the trachea and the substernal pres ence of the goiter. Barium swallow will sho displacement of the esophagus. Needle biopsy o the thyroid is not recommended unless Hashi moto's thyroiditis is suspected.

Surgical Experience

The surgical experience of the surgeon or th institution is to be considered in deciding fo elective thyroidectomy. In our experience th mortality rate for thyroidectomy is 0.1% and th morbidity rate is low (permanent tetany 0.3% and unilateral vocal cord paralysis less than 1%) These figures are sufficiently low to justify elec tive surgery. On the other hand, with morbidity rates significantly higher, selection of goiter fo thyroidectomy must be stricter and less frequently recommended.

The extent of surgery is based on the pathologic findings. For a discrete nodule confined to one lobe and proved to be benign on gross inspection and study of frozen sections, partial lobectomy is sufficient on the side of the lesion if the opposite side is normal. For bilateral benign lesions or for thyroiditis, bilateral subtotal resection with removal of the isthmus is indicated, leaving a thyroid remnant of 1 to 2 gm of tissue on each side of the trachea. When papillary adenocarcinoma is found, total lobectomy on the side of the tumor should be done as well as partial lobectomy on the opposite side since 20% of these cancers are multicentric. For extensive papillary lesions (extrathyroidal or multicentric cancer invading both lobes), total thyroidectomy should be considered. About half of these lesions will metastasize to cervical lymph nodes; modified neck dissection should then be done. Radical neck

dissection is indicated only when metastatic nodes are extensive (10% of cases with positive nodes).

For follicular adenocarcinoma, total lobectomy on the side of the lesion is indicated, and if there is evidence of blood vessel invasion or distant metastasis, total thyroidectomy should be done to prepare the patient better for radioactive iodine therapy, if and when it is necessary. Lateral neck surgery is infrequently indicated, since this tumor rarely spreads to the regional lymphatics. Medullary adenocarcinoma is multicentric in origin in a high incidence of cases and is more aggressive as cancer. For these reasons total thyroidectomy should be done. Prognosis for this tumor is related to the presence or absence of regional lymph node metastasis. Therefore, radical neck dissection should be done if nodes are considered positive for metastasis or if the primary lesion is considered aggressive. Anaplastic cancer of the thyroid is best treated aggressively although cure is infrequent. An adequate airway should be established if at all possible.

Summary

Nodular goiter should be selected for thyroidectomy on the basis of many factors, including history, physical findings, laboratory results, and the experience of the surgical practice. With careful selection, approximately 20% of nodular goiters recognized clinically will require surgical treatment. About 10 to 15% of these goiters will prove to be cancer. The extent of the surgical procedure should be tailored to the pathologic findings of the goiter and, in the case of cancer, to the known biological behavior of the particular cell type.

Meeting

Hennepin County Academy of Family Physicians

The Annual Invitational Banquet of the Hennepin County Academy of Family Physicians will be held on Monday evening, November 20, 1972, at the Sheraton Ritz Hotel in downtown Minneapolis. A social hour will begin at 6:00 p.m. with dinner scheduled for 7:30 p.m. The Speaker will be Dr. Murray Banks, Adjunct Professor of Psychology at Northwood Institute, Midland, Michigan. His speech is entitled 'What to Do Until the Psychiatrist Comes!" and you won't want to miss his "witty, wise, rare magic." We invite, and encourage to attend, any physicians and their guests, both from the metropolitan and out-of-state areas, to an enjoyable evening at the Sheraton Ritz. Those wishing information or tickets, please contact Donald L. Wright, M.D., 3620 Central Avenue N.E., Minneapolis, Minnesota 55418, telephone 780-1151.

Dr. Stirling . . . was liked being a man of broad sympathies. In his rich Scotch accent, he could discuss with equal ability the flavour of whisky or of a sermon, and he had more than sufficient tact never to discuss either whiskies or sermons in the wrong place. . . . He listened very seriously to all that [his patients] said; he seemed to regard [every] case as the one case that had ever aroused his genuine professional interest; but as it unfolded itself in all its difficulty and urgency, so he seemed, in his mind, to be discovering wondrous ways of dealing with it; these mysterious discoveries seemed to give him confidence and his confidence was communicated to the patient by means of faint sallies of humour. He was a highly skilled doctor. This fact, however, had no share in his popularity, which was due solely to his rare gift of taking a case very seriously while remaining cheerful.*

*Arnold Bennett's: The Old Wives Tale (Book IV, Chapter III), 1911.

Dementia

A Clinical Approach

BURTON A. SANDOK, M.D.

THE PATIENT WITH failing mental function poses for the physician a wide array of diagnostic considerations. If the patient is elderly and his symptoms have progressed slowly, frequently the tendency is to assume that the problem is one of a group of presenile or senile dementias[1] and to limit diagnostic evaluation. There are, however, potentially treatable forms of dementia; and this approach precludes the possibility of restoring mental function in these instances of reversible disease.

Clinical Approach

Seldom do patients with a dementia present complaining of mental change. Other family members note some change in the patient's behavior and persuade him to seek medical aid.

The patient often comes to the physician with somatic problems that poorly fit the more typical patterns of physical disease. In eliciting the history, which at times is vague, unclear, and imprecise, the clinician may suspect mental alteration. He should always try to confirm this impression by consulting other family members.

Faced with such a problem, the physician must plan his evaluation to answer two basic questions: (1) Does the patient have a dementing process? and (2) If so, what is the cause? That is, is it a potentially treatable (arrestable or reversible) form of dementia or one not likely to respond to specific therapy?

Initial Clinical Classification

A useful clinical classification is outlined in Table 1.

Several functional alterations in mental processes may superficially resemble a dementia.[2] Depression is the most frequent in this category because the accompanying mental lethargy and psychomotor retardation are often construed as diminished mental capacity. Patients with focal neurologic disorders, especially those who are unable to cope with their environment owing to faulty processing of language (dominant hemisphere disease) or faulty perceptual orientation (nondominant hemisphere disease), may seem perplexed and confused; the difficulty is often interpreted as a dementing process. Such deficits may be prominent in a diffuse dementia, but when such abnormalities exist in isolation, one must be alert to the possibility of a focal structural lesion.

The patient may notice the subtle changes and failing mental processes associated with an early dementing process and react to these changes in accord with the dictates of his own personality. Although depression is common, other behavioral aberrations may be seen. Though the presenting symptoms seem appropriate to a functional disorder, these may merely be reactions to an organic deficit. The clinician should seek evidence of a dementing process in any patient with recent personality change, regardless of the superficial symptoms.

In some patients dementia is merely one aspect of a more obvious systemic or neurologic disease. In such patients differential diagnosis or management is seldom difficult.

There remains, however, a significant number of patients in whom, after careful clinical examination, no evidence of underlying disease can be

TABLE 1
Dementia: Initial Clinical Classification

Pseudodementia: disorders that may mimic dementia
- **Functional states: depression, dissociative states, anxiety, hysteria, etc.**
- **Focal neurologic disease: specific language deficits (dominant hemisphere disease), disorders of visual-spatial orientation (nondominant hemisphere disease)**

Pseudo-pseudodementia: disorders presenting primarily as functional states, but which are merely a reaction to an underlying organic process

Dementia with obvious associated disease

Dementia without obvious associated disease
- **Potentially treatable disorders**
- **"The rest"**

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See editorial, page 913.

detected. In most of these patients change is irreversible; and there is a tendency, in the elderly patient, to accept arteriosclerotic cerebrovascular disease as the usual cause. It must be pointed out that current studies suggest that there is no precise relationship between dementia and underlying vascular disease.[3] In some patients the mental change can reflect an underlying, potentially treatable disease, which can benefit from specific therapy. The clinician is obligated to ascertain whether such a disorder is present before committing the patient to live out his years with significant disability.

Clinical Examination

No specific test enables the physician to diagnose a dementia. While talking to the patient he must be able to recognize those features of an organic brain syndrome which seem to be common to all patients with a dementia, regardless of specific cause (Table 2). These symptoms are superimposed upon the patient's previous personality, environmental situation, current emotional stresses, and those symptoms attributable to the specific etiologic agent responsible for the impairment of brain function.[4]

TABLE 2
Dementia: Clinical Features

Common basic features (mnemonic = JOMAC)
- **Impairment of**
  - **Judgment**
  - **Orientation**
  - **Memory**
  - **Affect (and abstraction ability)**
  - **Calculation (and comprehension, concentration, and other intellectual functions)**

Impairment superimposed on symptoms relating to
- **Previous personality**
- **Environmental factors**
- **Current emotional stresses**
- **Specific etiologic agent**

The clinical examination differs little from that required for any patient presenting for a general physical examination. But the ease with which a mildly demented patient can relate the history and appear to be mentally quite intact is deceptive. The defect of mental functioning becomes apparent only when the patient is stressed with the unfamiliar or the uncommon. Therefore the answers to simple questions directed at testing speech and language ability, recent memory, judgment, calculation, orientation, and fund of knowledge are likely to be revealing. A complete general physical examination, including a survey of neurologic functioning, should be made.

Clinical Diagnostic Considerations

Table 3 outlines the management based on diagnosis. For those patients with a dementia, but who also show symptoms and signs of systemic disease (group C), the approach is that of evaluating the underlying disorder. For those with abnormalities in both the neurologic examination and mental function (group D), appropriate neurologic referral seems indicated. If there is no obvious associated disease and there is still a question as to whether a dementing process is present (group B), psychologic testing should be done. If there is no evidence of a dementia (group A), reassurance and understanding are frequently beneficial; however, psychiatric referral is warranted if significant psychopathology is evident.

TABLE 3
Dementia: Diagnostic Conclusions and Approaches to Management

Group	Diagnostic Conclusion	Management Approach
A	No dementia present; functional disorder likely	Reassurance; psychiatric referral if indicated
B	Dementia possibly present	Formal psychologic testing should be obtained to confirm or deny the presence of a dementia
C	Dementia present, but secondary to obvious systemic disease	Evaluation and treatment of the primary disorder
D	Dementia present; possibly secondary to a focal cerebral lesion	Appropriate neurologic evaluation
E	Dementia present; no obvious evidence of underlying systemic or focal neurologic disorder	Obtain screening tests, for occult, but possibly treatable cause Consider further diagnostic study if indicated

The remainder of patients consist of those with an obvious dementia, but in whom there seems to be no significant associated systemic or neurologic disease. Table 4 lists some of those disorders in which dementia may be the initial (or most prominent) manifestation, and in which specific therapy can effect remission of some of the mental symptoms. Review of this listing suggests that most of these diseases can be detected (or at least suspected) by a careful history and clinical examination supplemented by selection of basic laboratory tests aimed at uncovering these disorders.

Roentgenography of the head supplemented by electroencephalography and radioisotope scanning occasionally reveal *focal brain lesions* not evident after neurologic examination. A hematologic survey, tests of metabolic function, and chest Xray should also be obtained.

The association between *thyroid dysfunction*

and mental change is well recognized.[5] Since these mental changes may develop in the absence of other obvious clinical signs of myxedema or thyrotoxicosis, evaluation of thyroid function is important in an unexplained dementia.

TABLE 4

Dementia: Potentially Treatable Causes*

Neoplastic disorders	Brain tumor (frontal lobe, intraventricular, etc.)
Endocrine disorders	Thyroid, parathyroid, and adrenal; dysfunction; hypoglycemia
Other metabolic disorders	Hepatic, renal, pulmonary insufficiency
	Hyponatremia
	Porphyria
	Wilson's disease
Exogenous toxins	Drugs (barbiturates, bromides); heavy metals
Deficiency states	Hypovitaminosis B_{12}
	Wernicke-Korsakoff syndrome
	Pellagra, etc.
Vascular disorders	Post-subarachnoid hemorrhage with hydrocephalus
	Secondary to sustained hypertension
	Systemic lupus erythematosus
Post-traumatic disorders	Subdural hematoma
	Communicating hydrocephalus
Inflammatory disorders	General paresis
	Brain abscess
	Meningoencephalitis, chronic
	Postinflammatory arachnoiditis with hydrocephalus
Miscellaneous conditions	Recurrent seizures
	Hematologic disorders
	Remote effect of carcinoma

*Partial listing only.

Mental change has long been known to be a common accompaniment of *pernicious anemia.*[6] Patients with B_{12} deficiency having dementia but having no other signs of the classic disorder nor evidence of anemia have been reported.[7] Neither the absence of anemia nor obvious morphologic change in the blood smear appears sufficient to rule out this disorder, and specific testing (Schilling test, serum B_{12} assay) seems indicated.

Central nervous system *syphilis,* once a prominent cause of dementia, is still encountered; appropriate serologic testing is mandatory.

Dementia, associated with communicating *hydrocephalus,* is a potentially treatable disorder[8] which may follow conditions such as subarachnoid hemorrhage, trauma, and chronic meningitis or may arise without apparent antecedent cause. The characteristic picture includes dementia, apathy, gait disturbance, and urinary incontinence.[9] The differential diagnosis of this disorder involves other considerations including that of an intracranial space-occupying lesion.

Examination of cerebrospinal fluid may prove necessary; however it should be deferred in most patients with evidence of focal neurologic abnormality for it may interfere with other tests, such as radioactive cisternography and pneumoencephalography.

Conclusions

A patient presenting with symptoms suggestive of a dementia may have one of a variety of disorders. Frequently one is inclined to regard the dysfunction as symptomatic of a group of ill-defined diseases of the senium and presenium and to limit evaluation. There are several not uncommon disorders that may present as a dementia and that may be reversed once appropriate therapy is instituted.

A systematic approach to the investigation of a patient presenting with a dementia enables the clinician to discover potentially reversible causes of dementia and to administer specific therapy.

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*Shall such a beggar's brawl as that, thinkest thou, make me a thief? The pox light on her whore's sides, a pestilence and a mischief!**

*Gammer Gurton's Needle: Acti II scene ii. 1575.

Injuries of Knee in Athletes

FRANKLIN H. SIM, M.D. AND LEE C. DETENBECK, M.D.

PHYSICIANS ARE TAKING increasing interest in sports medicine. Many are actively engaged in the prevention, diagnosis, and care of injuries of athletes. Because the knee is the joint most easily injured, a sound understanding of its functional anatomy[1] and the associated clinical problems is important.

Stability of the knee depends on static and dynamic elements. The static support includes the medial and lateral collateral ligaments, the posterior capsule with its ligamentous thickenings, and the strong fan-shaped cruciate ligaments. All act synergistically to prevent abnormal lateral, rotatory, and anteroposterior motion. The most important dynamic stabilizer is the powerful quadriceps extensor mechanism. Other dynamic stabilizers are the hamstring muscles, the two heads of the gastrocnemius, and the popliteal muscle. In addition, the medial and lateral menisci and the joint articular surfaces must be intact to allow stable, smooth knee motion.

Proper physical conditioning and muscle strengthening prior to participation in strenuous sports are of paramount importance in preventing injuries. Knee injuries may present to the physician early or late. Diagnosis is much easier if the knee can be examined immediately after injury, before significant pain, spasm, and swelling develop. If the ligaments, menisci, articular cartilage, and quadriceps extensor mechanism are remembered when examining the knee, most traumatic lesions can be diagnosed clinically.

Ligamentous Injuries

The most disabling knee injury is rupture of the medial collateral ligament. The medial ligament consists of a long superficial portion and a shorter deep capsular portion that is attached to the medial meniscus. Brantigan and Voshell,[2,3] and more recently Slocum and Larson,[4] have contributed most to our understanding of this functionally important structure. The latter authors also stressed the importance of the entire medial capsule of the knee, extending from the popliteal space posteriorly to the patellar tendon anteriorly.

The position of the knee at the time of injury determines the anatomic defect. In extension the posteromedial capsule becomes taut and the superficial portion of the tibial collateral ligament moves forward and tightens. With 30° to 60° flexion these structures are relaxed and stress is applied to the taut meniscofemoral and meniscotibial portions of the deep medial capsular ligament. The anterior third of the capsule, which is reinforced by the retinaculum of the vastus medialis, is tightened passively when the knee is flexed. Combined rotatory and abduction stress, when severe, gives rise to concomitant injury to the medial meniscus and anterior cruciate ligament completing O'Donoghue's unhappy triad.

As stated previously, the most important factor is early examination, for it is then that the physician can best determine the integrity of each of these structures in the knee. Determination of the exact sequence of events leading to the injury will give some idea about its severity, especially if the athlete can give an accurate description of how the injury occurred. Most frequently the foot is fixed to the ground. The thigh rotates inward, the foreleg outward, and the knee is forced medially with primary stress on the medial ligaments and capsule. This is commonly caused by the lateral blocking maneuver in football or when a player falls on the outstretched leg. These injuries also may occur in noncontact activities such as running, where the foot is forced into external rotation and stress is exerted against the medial ligament. If an athlete has immediate pain but is not disabled, can bear weight, and walks off the field, the symptoms are suggestive of partial rupture of the ligament. Gradual progression of pain, swelling, and restriction of motion may follow. The sequence of events suggestive of more extensive ligament damage includes inability of the patient to bear weight and the development of early severe pain, swelling, and ecchymoses.

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Treatment of the ligament injuries depends on the severity.[5] With a mild injury and no loss of ligament strength, prompt resumption of activity may be allowed after the local reaction subsides. If the sprain is of moderate severity, that is, the ligament is partially torn but no lateral instability is noted, treatment includes: compression, ice packs, aspiration and local injection, protection in a cylinder cast, and rehabilitation. In complete ligamentous disruption, lateral instability is evident (Figure 1 A). A palpable defect in the ligament may be present and often a "vacuum sign" or local invagination of the skin which is caused by negative intra-articular pressure as the joint is sprung open. When the integrity of the ligament is in doubt, we do not hesitate to examine it under general anesthesia.

When ligamentous disruption is ascertained, exploration of the knee with repair of the ligaments and excision of a torn meniscus is done to prevent residual instability[6,7] (Figure 1 B). Management of the torn anterior cruciate ligament is more controversial. If it is detached from the tibia or femur, it should be repaired through drill holes in the bone. If it is torn and attenuated in its midportion, repair is difficult and often unrewarding. In these instances, we frequently excise the ligament and repair only the medial collateral ligament. With adequate strengthening of the quadriceps, few patients note any disability but resumption of *strenuous athletics* is often impossible. Primary ligament repair, when feasible, is always preferable.

Rotary instability[8] or abnormal increased outward rotation of the tibia on the femur may be disabling to the athlete. The basic lesion that permits this external rotation of the tibia is injury to the deep medial capsular ligament. Instability in lateral movement is noted especially when cutting away from the supporting foot. In order to control this rotary instability, the muscles of the pes anserinus tendon (sartorius, gracilis, and semitendinosus muscles) are transplanted along the medial aspect of the patellar tendon and medial flare of the tibia, converting these muscles from primary knee flexors to internal rotators of the tibia (Figure 2).

Injuries to the Menisci

The term "internal derangement" describes a



Fig. 2—The inferior two thirds of the pes tendon has been detached, reflected, and re-attached to the tibial tubercle and margin of the tibia.

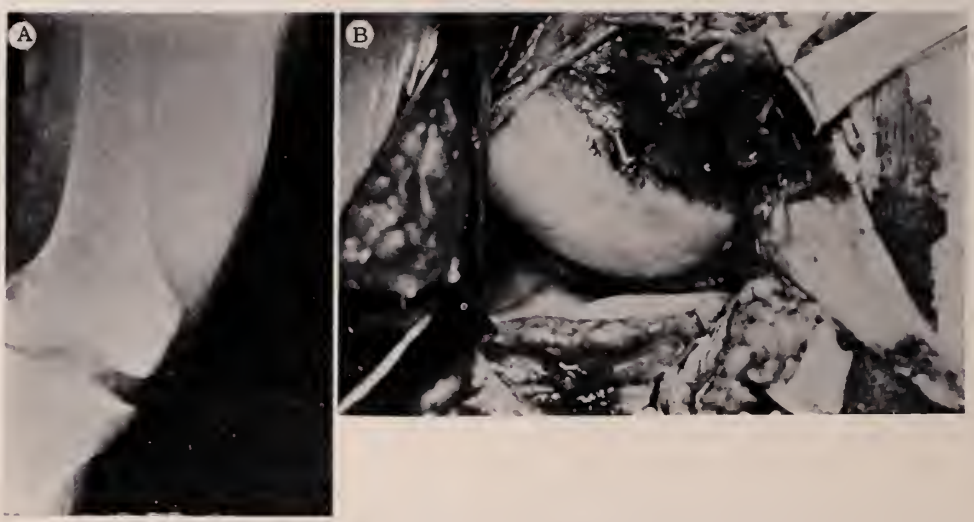


Fig. 1—(*A*) Anteroposterior view of knee under stress showing lateral instability. (*B*) Torn medial collateral ligament showing superficial and deep portion of ligaments torn at joint line and held by retractor. The layers were repaired separately with anatomic approximation.

broad syndrome in which normal motion of the knee is impeded. Injuries of the menisci are common among athletes whose knees are subjected to strong rotational forces, especially when the foot is fixed to the ground and the knee is flexed. A portion of either the medial or lateral meniscus becomes displaced beneath the corresponding femoral condyle; and, as the knee extends, the meniscus is impaled and torn. Clinically, injuries to the meniscus may vary depending on the extent

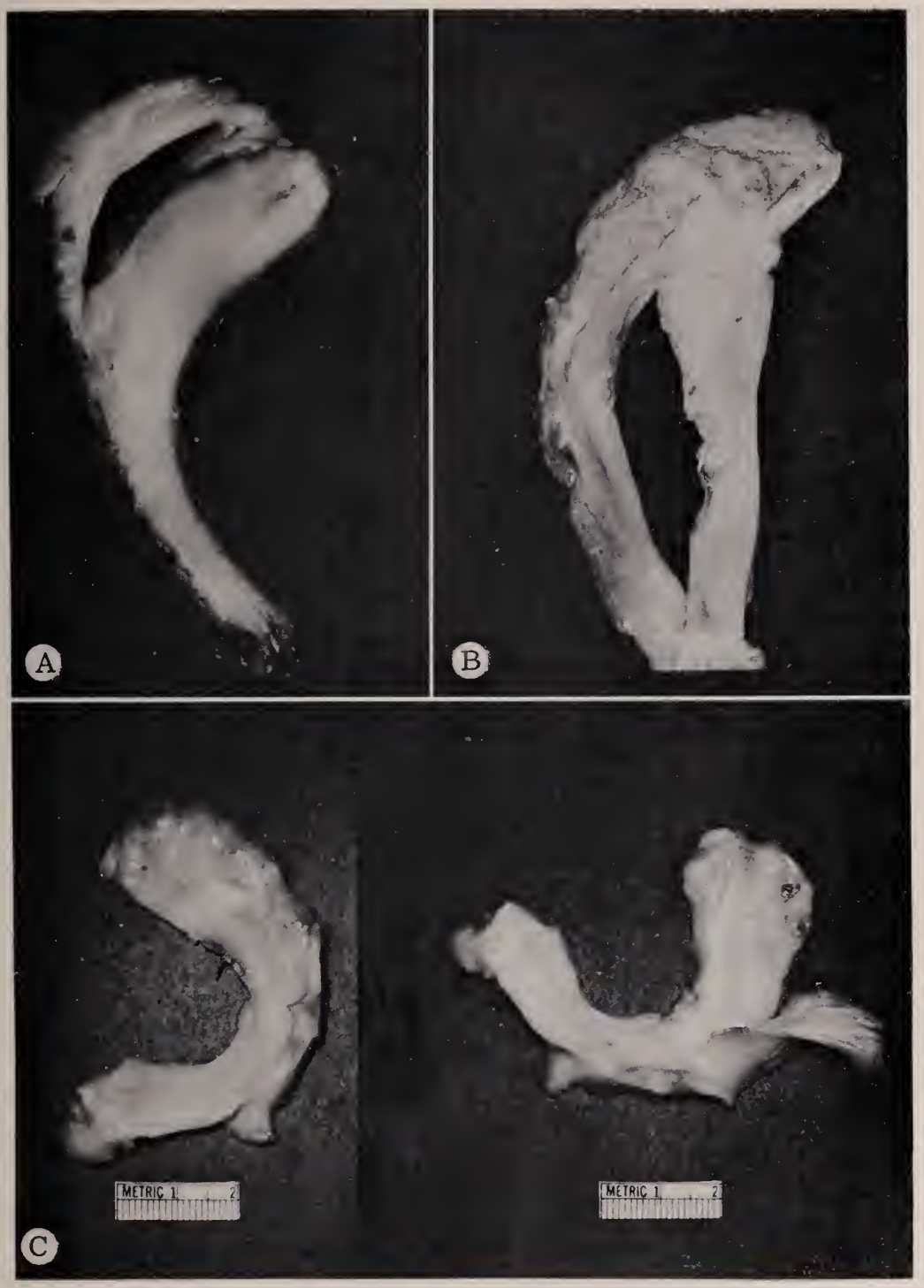


Fig. 3—*(A)* Longitudinal tear of posterior horn, medial meniscus. *(B)* Bucket-handle tear, medial meniscus. *(C)* Degenerative horizontal tear, posterior horn, medial meniscus.

and location of the tear. A description of the mechanism of injury may be helpful because symptoms often are manifested only during increased activity, such as cutting and pivoting maneuvers. With a longitudinal posterior horn tear (Figure 3 A), recurrent episodes of "giving way" associated with pain and effusion develop. Jointline tenderness and a palpable click may be detected in the various flexion and rotation maneuvers described by McMurray.[9] No locking occurs unless the tear extends anteriorly beyond the collateral ligament. When this occurs (Figure 3 B), the medial torn segment may become caught by the condyle which prevents it from returning to its normal position and gives the clinical picture of locking short of full extension.

The older athlete engaged in skiing or jogging often will present with a painful grinding sensation suggestive of a degenerative horizontal cartilage tear (Figure 3 C). A tear of the anterior horn is commoner among older patients than among younger persons. Locking is absent and the diagnostic maneuvers of McMurray[9] are negative. Disruption of the meniscus is the commonest cause of a traumatic knee effusion, and medial tears of the meniscus are approximately five times commoner than lateral tears.

Injuries to the Articular Cartilage

Injuries to the articular cartilage of the knee[10] comprise an important segment of injuries under the broad diagnosis of internal derangement. Frequently, arthrotomy for a disrupted meniscus will reveal an articular cartilage lesion as the true source of symptoms. The femur, tibia, or patella may be involved as a result of rotational stress, patellar subluxation, or direct violence. Lesions in this group consist of chondral fracture, osteochondral fracture, avulsion fracture, osteochondritis dissecans, or chondromalacia. Unlike a chondral fracture, an osteochondral fracture has a segment of underlying subchondral bone which is visible on ordinary roentgenograms. If the situation warrants, an osteochondral fracture may be reduced and fixed with a nail, K-wire, or screw (Figure 4). Osteochondritis dissecans should be considered in younger athletes who complain of aching in the knee with use and less often at rest. Recurrent effusion with activity may be noted and in some cases the fragment may fall in and out of the crater producing symptoms of intermittent locking.



Fig. 4—Osteochondral fracture of medial femoral condyle (left knee); fracture fragment repaired and held with Smiley nails.

Injuries to the Quadriceps Extensor Mechanism

In evaluating athletic injury to the knee, the quadriceps extensor mechanism must not be overlooked.[11] Lateral dislocation or subluxation of the patella occurs when the knee is flexed, externally rotated, and subjected to valgus stress. The line of action of the quadriceps is then lateral to the patella causing it to slide tangentially across the lateral femoral condyle. The misconception that patellar dislocation or subluxation occurs primarily in young women with "knock knees" or with a hereditary disposition has frequently caused this condition to be overlooked in male athletes. Symptoms and signs of patellar subluxation closely simulate lesions of the meniscus and many patients have undergone meniscectomy only to have continued disability until the correct diagnosis was made. Vague symptoms of pain or swelling or sensations of giving way or locking may be present. Often symptoms develop at the beginning of a game, before the athlete is limbered up, or the day after strenuous competition. On examination with the knee flexed, a lateral position of the patella in the groove of the anterior femur is seen. When bilateral, Hughston[11] refers to this as the "owl's eye" sign. A deficiency of the vastus medialis is usually obvious in knees with recurrent patellar subluxation. Lateral displacement of the patella with the quadriceps relaxed gives the patient a feeling of acute anxiety and he resists this maneuver. This is referred to as the "apprehension sign." Symptoms of patellar chondromalacia

lso may develop. Tangential views often will ıow the lateral position of the patella in the roove and a deficiency of the lateral femoral ondyle. Initial treatment is progressive resistive xercises for the quadriceps muscle. If symptoıatic subluxations persist, surgical procedures are ecessary to restore proper alignment of the exensor mechanism. The tight lateral retinaculum s released, the medial retinaculum is imbricated, nd often the patellar attachment is transferred ıedially.

In any injury of the knee, proper treatment includes a carefully supervised rehabilitation program until maximal recovery is attained. Return to strenuous athletics should not be allowed until the physician and patient are both satisfied that recovery is complete.

Summary

Knee injuries in the athlete are common. Early and proper diagnosis followed by adequate treatment and rehabilitation are necessary for maximal recovery. The commonest injuries are those of the ligaments, menisci, articular cartilage, and quadricep extensor mechanism.

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Cover Photograph

"Mayowood"

The original land in the estate of Dr. and Mrs. Charles H. Mayo was purchased shortly after 1900 as a small acreage and the area gradually grew to more than three thousand acres which became known as Mayowood.

Construction of the house was started in 1910 and completed in the fall of 1911. The general architectural design of the house was largely the work of Dr. Charlie himself and the site was chosen because the present courtyard area was a favorite woods picnic spot for the family. The poured reinforced concrete construction necessitated the bringing to Rochester from Chicago one of the largest concrete mixers ever seen in this area.

For all the years since 1911, Mayowood has been a cultural and social center of the area. During the early years Dr. and Mrs. Charlie were the hosts and after 1940 Dr. C. W. and his wife Alice welcomed the many guests. Thirty-eight rooms are furnished with many lovely French, Spanish, English and American antiques.

In December 1965 the late Dr. and Mrs. C. W. Mayo gave their home and ten surrounding acres to the Olmsted County Historical Society. Since 1966 regular tours of the house have been scheduled. In June 1968 Mayowood was dedicated as a Minnesota State Historic Site by act of the 1967 session of the Minnesota Legislature. In 1970 Mayowood was named to the National Register of Historic Places.

Cryosurgery for Tumors of the Head and Neck

Experimental and Clinical Considerations

H. BRYAN NEEL III, M.D. AND L. W. DeSANTO, M.D.

Cryosurgery is an acceptable alternative to extirpative surgery, particularly in patients with neoplasms of the head and neck where classic resections produce losses of large portions of mandible or maxilla.[1-5] Profound cold predictably destroys benign or malignant neoplasms that are readily accessible, induces local anesthesia by rapid destruction of sensory nerve fibers, and produces hemostasis by injury to small blood vessels and capillaries.

Although cryosurgical techniques are applicable in all surgical specialties, little is known about the temporal and physical requisites for cryogenic control of cancer. Thus, we analyzed the clinical results and laboratory findings to determine the conditions of freezing required to consistently produce cell death in a target area. These data constitute the rationale for modern clinical cryotherapy.

Experimental Work

Cell Death by Freezing

Biologists have known for many years that repeated cycles of freezing and thawing produce a series of events that are lethal to cell suspensions in vitro. These events are: (1) temperature change (thermal shock), (2) formation of extracellular and intracellular ice crystals, (3) concentration of extracellular and intracellular solutes, and (4) cell shrinkage. Cells in vivo respond similarly to profound cold, but the circulation of blood, a continuous source of heat to the target area, variably and inconsistently changes the amount of cold required for cell death.

In clinical cryosurgery for cancer, the time required to destroy tumor is determined by its size. The iceball must extend at least one cm beyond the tumor into grossly normal tissues if all of the tumor is to be destroyed.[3] Tumor margins mus be accurately estimated to ensure that temperatur sensors are placed beyond the tumor, includin the deep side. A wide margin of normal tissu must be included within the area, just as a wid margin of normal tissue must be included in th specimen in the classic excision.

Temperatures Required for Cryonecrosis

It has often been stated that freezing to abou −20° C is adequate for complete necrosis of al tissues within the target area, but differential cel sensitivities to cold or variations in blood supply (or both) make that a marginal temperature a best.[6] This has been demonstrated repeatedly i several syngenic animal systems using viral an chemically induced tumors.[6,7] In these studies tumors of 1 cm in diameter and 0.5 cm of grossly normal adjacent tissues were included in the ice ball, thus eliminating variations in extent of freez ing. Because size of tumor, size of probe tip, an temperature remained constant, any differenees i tumor control would be due to other faetors depth of freeze, duration of freeze, rates of freez ing, and duration of thawing. In addition, when a large (80 sq mm) probe tip was employed, th possibility that changes in tumor boundary wer induced by movement of tumor cells in the ad vancing ice front was excluded because the tip-to tumor ratio was approximately 1:1. (Whether o not tumor cells move with the advancing ice fron is speculative.)

Freezing to tumor temperatures of −18° C an −44° C generally failed to control the tumor, bu freezing to below −44° C controlled the tumor i more than 90%* of animals studied. Similarly whether the tumor was frozen very rapidly (260 C/min) or less rapidly (100°C/min), one freez to −90°C was far more effective than one freez to −20° C. Duration of probe application prob ably has little bearing on tumor control becaus

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

*Tumor control refers to cure. Each group for which tumor control in percentage is cited consisted of 15 mice or more.

th time required to freeze to either terminal tumor tc perature at the slower rate was two to four ti es that at the more rapid rate. Optimally, these tuors should be frozen rapidly to well below -44° C and probably to temperatures of —60° C. In clinical cryotherapy, when a choice is re- q red between rapid freezing and low tumor tem- r ature (as with large tumors), the latter is the b ter alternative. Because freezing time increases v h tumor size, the freeze rate is reduced. Longer a lications of the probe will eventually reduce t temperature to the desired level.

Two and three freezes (repetitive cycles of f ezing and spontaneous thawing) of the same tumor are far more effective than one freeze. If t temperature of the probe tip approaches the b iling point of liquid nitrogen (−196° C), tu- r control increases from 50% after one freeze t between 83% and 100% after three freezes, d pending on the tumor-host system. With the s me probe tip at —60° C, one freeze cures 7% a animals whereas three freezes cure 42%. T erefore, cryosurgical systems that employ cool- g agents other than liquid nitrogen probably w uld be ineffective for cancer control.

ffects of Repeated Freezing and pontaneous Thawing

Repetitive freezing can simply enlarge the ice- all.[8] However, in the mouse-tumor studies the end oint of freezing was determined by extension of e visible iceball 0.5 cm beyond the margins of e tumor into grossly normal tissues. Hence, the ze of the iceball was constant and determined the uration of freezing. Tumor control was dependent ot on the size of the iceball but on the conditions f freezing within the frozen mass. In studies of ormal liver, local temperature measurements ere obtained, and depth of freezing and duration f thawing were both increased by repetitive freez- g. Rapid freezing and slow thawing encourage ecrystallization and formation of larger, more table ice crystals. These effect cell destruction nd ischemia, resulting in necrosis.

Probe Contact with the Tumor

When the surface of the probe tip makes con- act with most of the exposed surface of the umor, all other conditions of freezing being equal, umor control is most effective. At —180° C, a probe tip with a tip-tumor contact ratio of about 1:1 produced cures in 82% of animals studied, whereas a tip-tumor ratio of one fourth that size produced cures in only 54%.

The Effects of Ischemia in Cryosurgery

Because blood is a continuous source of heat to the target area, limitation or exclusion of blood flow should potentiate cryonecrosis. Temporary ischemia, induced in the liver by clamping the porta hepatis, quadruples the volume of cryonecrosis and assures death of all cell types within the target.[9] With temporary ischemia, tumor implants in the livers of syngenic rats were successfully eradicated by repetitive cryoprobe applications.[10]

Clamping is impractical and often not feasible in many anatomic regions. Therefore, we evaluated tumor control after local injection of pharmacologic doses of epinephrine.[7] Subcutaneous fibrosarcomas in a syngenic murine system were frozen after local infiltration of epinephrine and clamping of the tumor vascular pedicle during freeze-thaw cycles. Tumor control in these two groups was compared with controls. No significant differences were observed between the two groups that underwent ischemia. Two freezes in the presence of ischemia were equivalent to three freezes without ischemia, producing tumor control in 95% of 40 mice. This represents not only a significant conservation of effort but also a marked potentiation of heat extraction, all other conditions being the same. Whereas small increases in depth of freezing were produced, thaw time was clearly prolonged. Passy et al.[11] found that injecting epinephrine in saline beneath the oral mucosa of dogs prior to cryoprobe application significantly enhanced cryonecrosis of these tissues. Indeed, all data indicate that local administration of epinephrine prior to cryosurgery markedly potentiates the effects of cryosurgery and may be a useful adjunct to cryogenic treatment of neoplasms in patients.

Immunologic Considerations

Cryosurgery and cryonecrosis produce a definite and specific antibody response to normal tissues and tumor. This has led to the term "cryo-immunization."[12] Among normal tissues, the coagulating gland of the rabbit has been most extensively studied. After cryonecrosis in situ, circulating antibody specifically directed against components of that organ has been detected by passive hemagglutination and gel-diffusion techniques.[12] This auto-antibody is species- and tissue-specific. The antibody was detected in the serum within four days after cryotherapy, and the titers reached a maximal level by seven to 10 days. Antibody titers declined thereafter. Antibody ac-

tivity was predominately 19S early in the postoperative period; later, 7S activity was detected. This corresponds to the pattern observed after antibody induction in general. Subsequent cryotherapy of the same tissue led to a "booster" effect, with production of higher and more prolonged elevations of 7S antibody.

Of particular interest in the treatment of malignant neoplasms is the differential tumor-specific immune response observed after cryonecrosis of both viral and chemically induced tumors in several animal systems.[13] This apparently results from prolonged exposure to tumor-specific transplantation antigens as compared to complete excision. Consistently greater immunity was seen after tumor necrosis in situ by cryosurgery or by ligation of tumor than by tumor excision, and the magnitude of the immune response was the same after treatment by either method. This suggests that cryosurgery does not significantly alter tumor antigen(s) and that the immunologic effects are induced by mechanisms which involve rapid tumor kill in situ and subsequent absorption of tumor-specific antigens. The increased immunity seen after cryosurgery is consistently demonstrable in several murine systems and may also explain the striking tumor regressions reported after cryosurgery of human tumor.

The mechanisms of so-called cryo-immunization are not clear, but because cryosurgery and ligation appear to have equivalent effects, duration of host exposure to tumor-specific transplantation antigens in situ appears to be a factor. Both techniques lead to ischemic necrosis and delayed slough of tumor 1½ to 2½ weeks after treatment. Necrosis may produce molecular changes in antigen or may liberate normally sequestered antigens into blood, lymph or both. Antigen release can be induced by immune complex formation and cell lysis in the presence of complement.

It has been impossible to produce regression of established tumors by immunologic means alone, but in the near future, immunotherapy may become an important adjunct to surgery. Because tumor-specific antigens have been demonstrated in many human tumors, the immunologic response of patients to cryotherapy of cancer should be studied.

Clinical Cryosurgery

At the Mayo Clinic DeSanto[3] has recently reviewed the results of cryotherapy in 44 patie with neoplasms of the head and neck regi Eight patients with squamous cell carcinoma w treated for cure, and 27 (most with squam cell carcinomas) were treated for palliation. Cr surgery was employed as an adjunct to excisio surgery in nine patients with nonmalignant mors: two with angiofibromas of the nasophary six with squamous papillomas of the larynx, a one with a hemangiopericytoma involving nose.

Technique

All cryosurgery is performed in the operati room with sterile technique. A self-pressuriz cryosurgery unit, which utilizes liquid nitrogen heat extraction (Brymill model SP5), is used, a the choice of cryoprobe depends on the site, si and accessibility of the tumor. Open-tip spr probes are used for lesions involving the anter oral cavity, for mobile portions of the tongue, a for those within maxillectomy cavities. Gros normal tissues beyond the target site are p tected by insulation with Styrofoam and Vaseli impregnated gauze. Closed probes are used lesions involving the base of the tongue and hyp pharynx. These probes are applied to the surfa of the tumor or inserted into it.

Tissue temperatures are continuously monitor by needle thermal sensors placed one to two from the gross margins of the tumor. Tumors a frozen repetitively, at least three times, and lowed to spontaneously thaw prior to refreezir When closed tips are employed, repetitive pro applications at several sites are necessary to ad quately freeze tumors larger than four cm diameter.

Recently, probes have been developed wi small apertures that allow spraying of the targ with liquid nitrogen. Although open-tip spr techniques effect cryonecrosis of more tissue in shorter time, sprays are difficult to contr Chandler and Hiott[2] reported that closed pro tips of about one cm diameter are ideal for mc carcinomas of the oral cavity.

The operative procedure is generally carried o with patients under general endotracheal anesth sia. Patients with accessible cancers involving t mucous membranes of the anterior oral cavity a patients with recurrent cancers in maxillecton cavities are often anesthetized with intraveno analgesic agents.

Clinical Application and Outcome

Deeply infiltrating tumors with poorly defined margins are seldom suitable for cryosurgery. Because the margins of such neoplasms are cryptic, extensive freezing is required and several weeks pass before the eschar sloughs and the depths of the wound can be evaluated for residual tumor.

Tumors caudal to the tonsillar fossa within the base of the tongue and in the hypopharynx are not suitable for cryosurgery because visualization of the entire tumor for probe applications is partial, at best. However, tumors of the buccal mucosa, retromolar trigone, floor of the mouth, mobile tongue, and the palate are particularly suitable for cryotherapy.

Osseous tissues are readily destroyed by repetitive freezing, so that cryosurgery is an attractive alternative to excisional surgery. Tumors that involve bone, such as those of the anterior floor of the mouth abutting the mandible or those of the hard palate, are ideal for treatment because they are the most accessible. Indeed, Marcove and Miller[14] have shown that cryosurgery can eradicate primary and metastatic tumors of bone.

Cryosurgery of large tumors of the oral cavity and pharynx produces edema which may lead to upper airway obstruction. The following case is illustrative:

A 78-year-old white man had a two by three cm exophytic carcinoma of the right retromolar triangle (figure). He was asymptomatic. Because excisional surgery would have required composite resection of regional tissues including the mandible, he refused operation. Cryosurgery was performed with the patient under general anesthesia, with liquid nitrogen spray freezing delivered through an open-tip probe. The tumor was frozen to below −30° C three times and allowed to spontaneously thaw between freezes. When the patient awoke from the anesthesia, he experienced a massive swelling of the tongue and lateral pharyngeal wall. The swelling led to upper airway obstruction, and he required an immediate tracheotomy. The tracheotomy cannula was removed five days later, and the patient's recovery was uneventful. He is free of disease 18 months after treatment.

Profound cold induces hemostasis, yet major hemorrhage can occur after cryosurgery. This hazard is seen most frequently in patients in whom irradiation or tumor invasion or both have compromised the viability of large vessels.[2,3] Gage et al.[15] studied the effects of complete freezing of arteries, including the femoral, carotid, and hepatic vessels and the abdominal aorta, in dogs. They found no arterial dilatation at any time after cryosurgery during the study period of one year. They saw no arterial thrombosis in large caliber arteries but observed it in branches of the hepatic artery. They concluded that cryotherapeutic techniques could be safely applied to tumors surrounding large blood vessels that supply vital organs.

As an agent for palliation, cryosurgery generally produces disappointing results. Relief of pain, reduction of bulky tumor masses, and reduction of bleeding are usually accomplished. However, three patients in DeSanto's[3] series required further therapy because of postcryosurgical bleeding, and one developed an oral-cutaneous fistula. In three other patients, cryosurgery for local recurrences after maxillectomy reduced the size of the tumor so that these patients were able to again wear maxillary prostheses.

Cryosurgery is a useful adjunct to excisional surgery of vascular neoplasms. The coagulation necrosis induced by profound cold produces vasoconstriction, stasis, and clotting within small vessels.[16] The target area may then be safely excised or curetted. This has been the experience in the two patients with juvenile nasopharyngeal fibromas and in the patient with the hemangiopericytoma involving the nose.

Of the eight patients with cancer treated for cure, seven have had complete tumor control during the observation period of six to 20 months. One died after carotid rupture and ligation one month after cryotherapy. Radiation or excisional therapy (or both) failed to control tumor in this



Figure—Exophytic squamous cell carcinoma (2 by 3 cm) involving the right retromolar trigone. Lesion was treated successfully by cryosurgery.

patient and in six others of the group.

In a series of 28 patients with oropharyngeal eaneer treated for eure, Chandler and Hiott[2] indueed eontrol of the tumor in 61%, but follow-up was less than two years in most eases. There was one operative death. Gage[4] reported that 17 of 25 (68%) patients with oral eaneer treated by eryosurgery had survived for two years or more, a survival equivalent to that after eonventional surgical therapy. There were no operative deaths. All tumors were staged before operation using the TNM elassifieation. Their results indieate that the ehanee of sueeess with eryosurgery, as with all forms of treatment, is related to the size of the lesion.

Summary

If malignant disease is to be eonsistently controlled by cryosurgery it is important to utilize low probe-tip temperatures, large probe tip-to-tumor eontact surfaees or liquid nitrogen sprays, repetitive probe applieations, spontaneous thaw between freezes, freezing to tumor temperatures below −30° C, and rapid rates of freezing. In perimental tumor-host systems, ischemia indu either by loeal administration of pharmacolo doses of epinephrine or by temporary clamp markedly potentiates the effeets of freezing a thawing. A definite tumor-specifie transplan tion immune response follows eryonecrosis tumor in situ. This exceeds the immune respo seen after exeision of tumor.

Cryosurgery is an aeceptable alternative extirpative surgery or radiation therapy in selec patients with oral and pharyngeal eancers. Ho ever, it should not beeome a standard method treatment for eaneer until the eure rate with t therapy can be compared with that of eonventio therapy for similar tumors. Tumors must aeeessible, and the likelihood for cure by cr therapy is related to the size of the neoplasm. F palliation, eryosurgery generally relieves pain a by redueing tumor bulk, permits deglutition a better oral hygiene. The eomplieation rate amo this group of patients is high.

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It's the Law

Postoperative Ileus

A patient was admitted to the hospital for removal of a small cyst from his kidney. After surgery he developed paralytie ileus. Six days after the surgery he vomited, aspirated and died related to a eondition of severe paralytie ileus.

Medieal experts brought in to testify agreed that a patient should not die as a result of postoperative ileus if standard medieal practiees were followed. Family of the patient was awarded $575,000 by a California jury in a suit against the physician and the hospital. The physician and hospital were deemed negligent in not summoning another physician when it beeame apparent that the treatment being rendered was ineffeetive.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Carlo v. Hutch (Cal. Super. Ct., Contra Costa Co., Docket No. 118707, Dec. 15, 1971). The Citation, 25:5, June 15, 1972.

Pyridoxine-Responsive Anemia

A Preleukemic Manifestation?

H. CLARK HOAGLAND, M.D. AND JAMES W. LINMAN, M.D.

PYRIDOXINE-RESPONSIVE anemia was first described by Harris and associates[1] in 1956 and is now generally recognized as a distinct entity, usually acquired. The manifestations of pyridoxine-responsive anemia differ from those of pyridoxine deficiency in experimental animals and infants; the latter states are characterized by dermatitis and convulsions and respond to physiologic doses of pyridoxine, whereas the pyridoxine-responsive anemias are not associated with systemic manifestations and pharmacologic doses are needed to induce hematologic responses. Harris and his colleagues[2,3] have reviewed 72 cases of pyridoxine-responsive anemia; variability within this group was striking, and only 25 of the 72 patients were considered to be typical of the prototype case. They stated that "none of the seventy-two patients with pyridoxine-responsive anemia has been found to have or to develop leukemia."[2]

Recently, it has been emphasized that acquired sideroblastic anemia may represent an early stage of a neoplastic process, that is, a preleukemic lesion.[4] There are a number of isolated reports of cases of "refractory anemia" terminating with acute granulocytic or myelomonocytic leukemia, and it has been suggested that there exists more than a coincidental relationship between these entities.[5-8] Since certain pyridoxine-responsive anemias are types of acquired sideroblastic anemia,[9] it might be expected that some of these patients would eventually develop leukemia.

During the past six years we have seen at the Mayo Clinic over 250 cases of "primary refractory anemia." The majority have had demonstrable iron-overload and ferrokinetic patterns of ineffective erythropoiesis. Most of these patients had therapeutic trials with pharmacologic doses of pyridoxine as well as other hematinics, without appreciable responses. Included in this group are five patients who had hypochromic-microcytic, pyridoxine-responsive anemias; in contrast to previously reported cases, three of these patients either had leukemic changes in their bone marrow at the onset of their anemia or developed them later. The fourth patient exhibited sufficient changes to be classified as preleukemia;[10] followup on this patient has been less than one year. Only one of these five patients had no evidence of leukemia; there was no followup in this case as he died four months after his initial examination, from causes unrelated to his anemia. The peripheral blood smears and bone marrow specimens in these cases were reviewed independently by three experienced hematologists who had no prior knowledge of the patients' suspected diagnoses; there was uniform agreement concerning the presence of leukemia.

Case Reports

Case 1

This 58-year-old man was referred to the Mayo Clinic because of progressive chronic obstructive lung disease of 25 years' duration. He had lost 11.5 kg. in weight over the preceding 12 months; he denied having anorexia, fever, or increased sweating. He was a thin, pale, chronically ill man who had obvious signs of emphysema. There was no hepatosplenomegaly or adenopathy. In addition to findings compatible with obstructive lung disease with a diffusion defect, laboratory studies demonstrated a hypochromic-microcytic, non-iron-deficient anemia with a hemoglobin of 10.5 gm/100 ml (see Table for additional laboratory studies). The bone marrow revealed normoblastic erythrocytic hyperplasia and was otherwise not remarkable. He was started on oral pyridoxine, 50 mg daily, and in two months his hemoglobin had increased to 14 gm/100 ml. Shortly thereafter, the patient committed suicide; an autopsy was not performed.

Case 2

This 76-year-old man was referred to the Mayo Clinic because of back problems resulting from an automobile accident some years before. He had been anemic for one year, had been given iron, but had not improved. Physical examination revealed moderate pallor, pigmentation of

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the skin, and significant hepatomegaly; the spleen was not palpable. A liver biopsy revealed hemosiderosis without significant cirrhosis. Pertinent laboratory findings are listed in the Table. The anemia was hypochromic-microcytic, and the bone marrow revealed erythrocytic hyperplasia with megaloblastoid features (Figure 1), plus an increase in blast cells and atypical megakaryocytes. He was given oral pyridoxine, 100 mg/day, with no response over a two-week period. He was then begun on 50 mg/day intramuscularly, and over the ensuing eight days his reticulocyte count increased from 1.7 to 11% and his hemoglobin from 6.2 to 8.2 gm/100 ml. Despite continued therapy for five months, his peripheral erythroid values fell and serial bone marrow examination continued to demonstrate changes of myelomonocytic leukemia with a predominant erythroleukemic component. Transfusions were necessary over the next three months, and he died elsewhere seven months later of an acute myocardial infarction. A partial autopsy did not include examination of the marrow.

TABLE

Summary of Laboratory Data

	Case 1	Case 2	Case 3	Case 4	Case 5
Leukocytes	8,000	4,000	5,000	5,500	6,200
Platelets	308,000	147,000	236,000	Incr	95,000
Leukoerythroblastosis	0	+	0	0	+
Anisocytosis	2+	3+	3-4+	3+	4+
Poikilocytosis	2+	3+	3-4+	3+	4+
Hypochromia	3+	2+	3+	2+	2+
Microcytosis	2+	0	3+	2+	2+
Hemoglobin electrophoresis	Normal	Normal	Normal	Normal	Not done
Serum iron, μg/100 ml	160	144	226	130	211

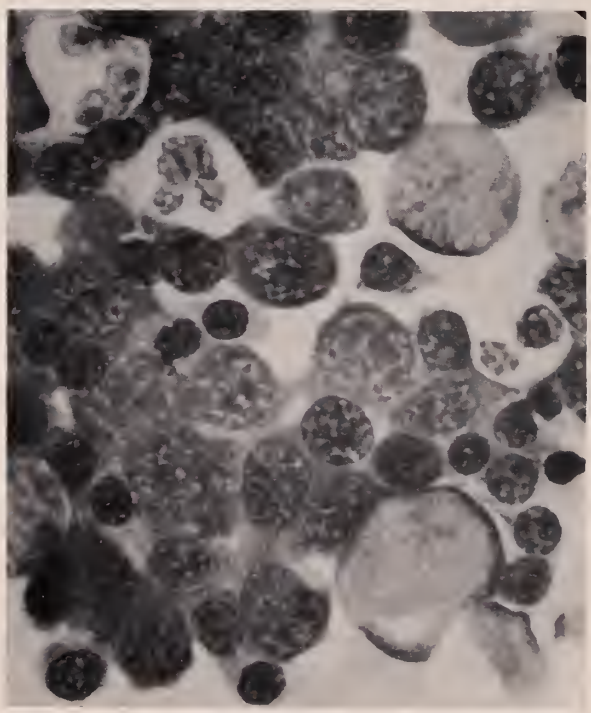


Fig. 1—Megaloblastoid erythrocytic hyperplasia with an increase in immature precursors in Case 2.

Case 3

A 77-year-old man, followed at the Mayo Clinic for many years because of arteriosclerosis obliterans, was first found to be anemic in April 1969, when he complained of increasing weakness and vertigo during the preceding two months. He was moderately obese. The liver and spleen were not palpable. Pertinent laboratory data are listed in the Table. The anemia was of the hypochromic-microcytic, non-iron-deficiency variety with a hemoglobin of 9.8 gm/100 ml. His bone marrow was hypercellular with an overabundance of immature megaloblastoid erythrocytic precursors together with such qualitative changes as increased numbers of siderocytes and sideroblasts, cloverleaf nuclei, and karyorrhexis (Figure 2). Several observers concluded that these changes were those of preleukemia. The patient was started on pyridoxine, 100 mg twice daily by mouth. Four months later, his hemoglobin was 13.7 gm/100 ml, with a red cell count of 3,840,000/cu mm. However, a repeat bone marrow examination still revealed clear-cut erythrocytic abnormalities with hyperplasia, maturation defects, and megaloblastoid features plus atypical megakaryocytes. These changes were again interpreted as those of an evolving myeloproliferative disorder (that is, preleukemia).

Case 4

This 49-year-old man, who had a long history of pemphigus, steroid-induced diabetes, and arteriosclerotic cardiovascular disease, was seen at the Mayo Clinic because of anemia of eight months' duration which had necessitated transfusion. Laboratory studies revealed a microcytic anemia with iron overload (hemoglobin 9.7 gm/100 ml) (see Table for additional laboratory data). The marrow was diagnostic of the erythroleukemic form of myelomonocytic leukemia (Figure 3). The patient was started on pyridoxine, 100 mg twice daily intramuscularly. Six days after pyridoxine was started, the reticulocyte count had increased to 8.3% and one month later the hemoglobin level was 13.0 gm/100 ml. Seven months later he died of a myocardial infarction, at which time the hemoglobin concentration was 10.8 gm/100 ml and the platelet count was 81,000/cu mm. A partial autopsy did not include examination of the bone marrow.

Case 5

This 44-year-old woman had a long history of discoid lupus erythematosus. Anemia had been noted prior to her examination at the Mayo Clinic. Treatment with a variety of hematinics including folic acid with vitamin B_{12} was unsuccessful, and periodic blood transfusions were required. Because of a hypochromic-microcytic, non-iron-deficient anemia with a hemoglobin of 7.0 gm/100 ml (see Table), she was given pyridoxine, 100 mg daily by mouth. Her hemoglobin level increased and there was no need for further transfusions. Two years later the anemia worsened and transfusions were again necessary to maintain satisfactory peripheral erythroid values. At this time, the bone marrow showed bizarre erythropoiesis with an increased number of blast cells, plus atypical megakarocytes (Figure 4), and was interpreted to be diagnostic of leukemia. Androgen therapy was begun (400 mg of testosterone enanthate once weekly), and five months later her hemoglobin level had

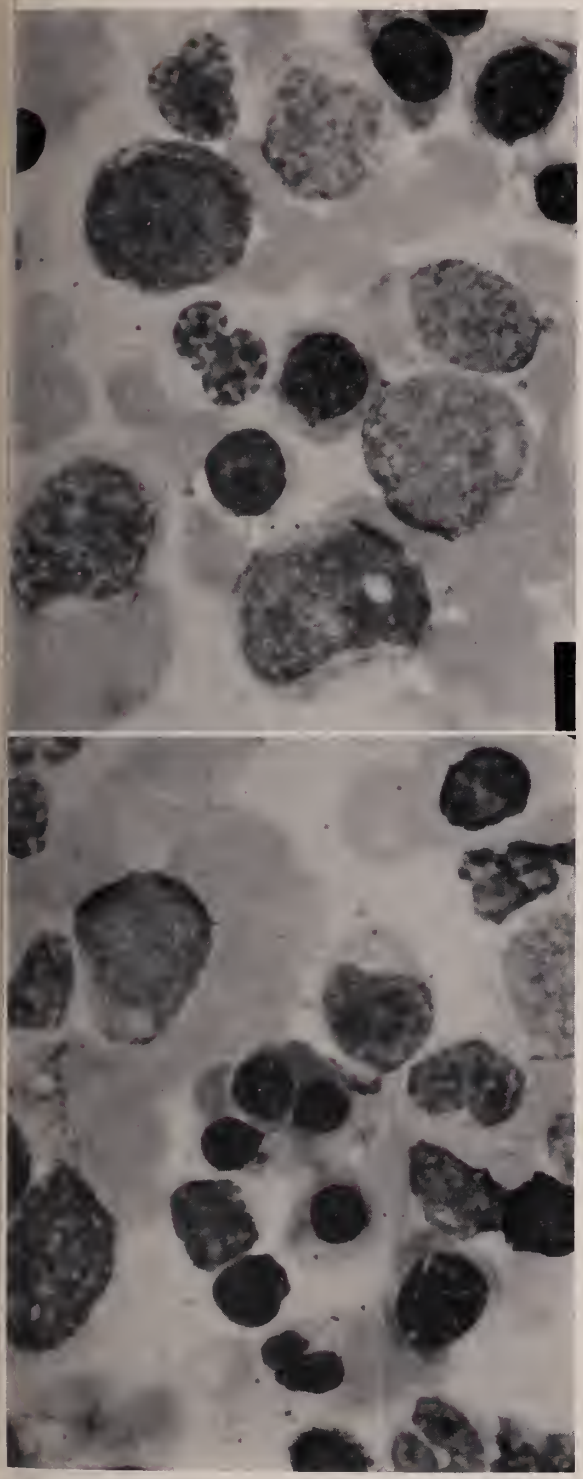


Fig. 2—Examples of marrow abnormalities in Case 3 (cloverleaf nuclei, megaloblastoid erythrocytic precursors, and maturation abnormalities).

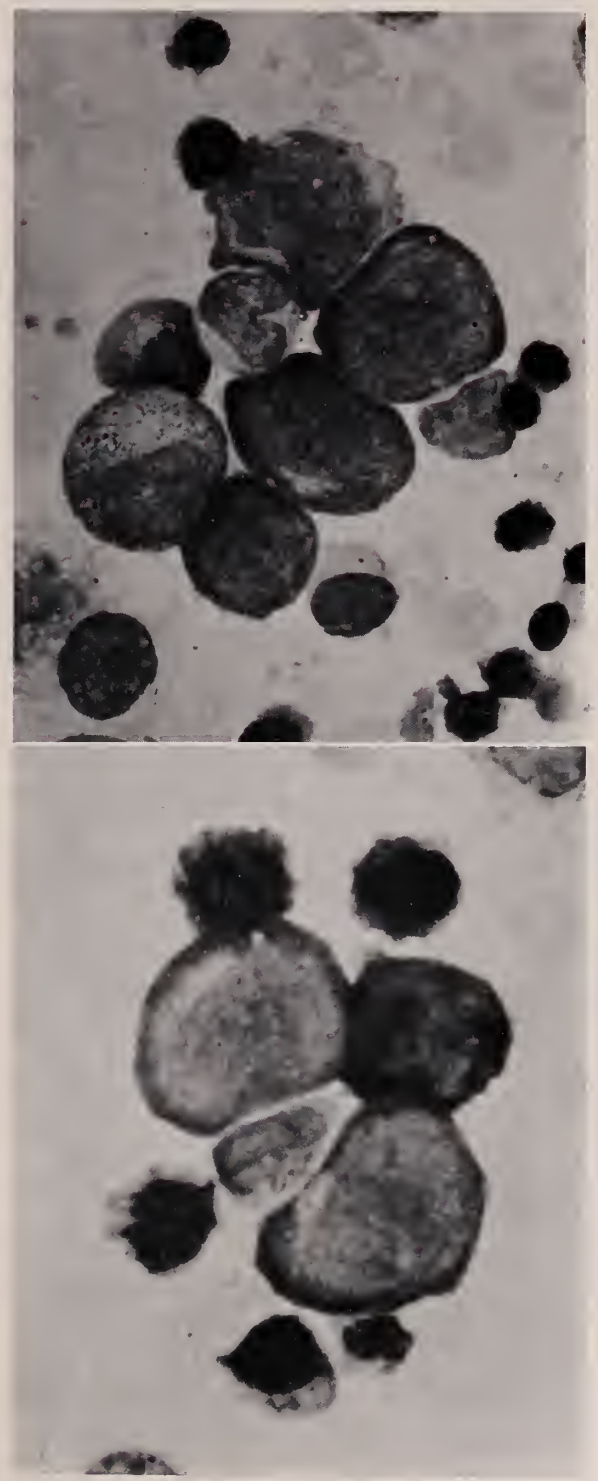


Fig. 3—Atypical erythrocytic precursors and overabundance of immature cells in Case 4.

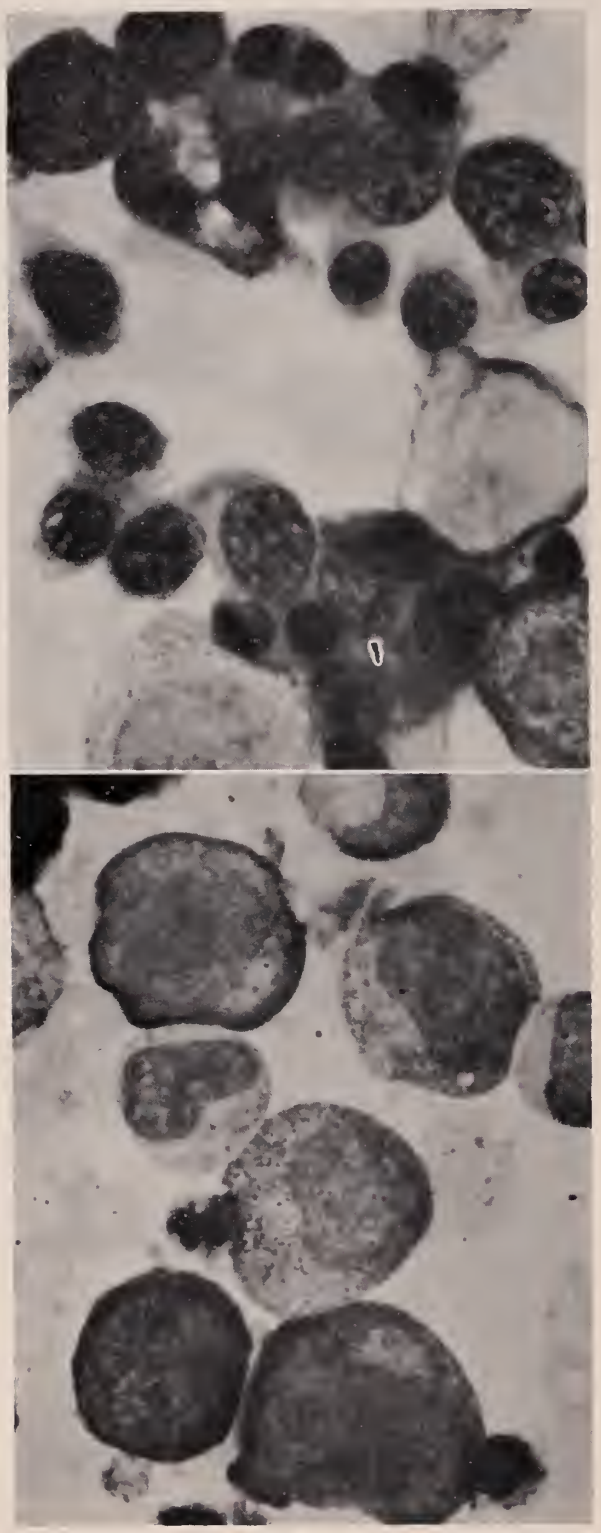


Fig. 4—Bizarre erythropoiesis with increased numbers of immature cells in the marrow of Case 5.

increased to 12 gm/100 ml; however, the qualitative abnormalities of her red blood cells persisted. She is still alive five years after onset of the anemia.

Discussion

All five of our patients were over 40 years of age, and four were men. Each presented with symptomatology directly related to anemia. All had normal leukocyte counts, and four had normal platelet counts. Two patients had evidence of leukoerythroblastosis in their peripheral blood. Each patient displayed marked anisopoikilocytosis with clear-cut hypochromia and microcytosis. Serum iron determinations were normal or elevated in every patient, and hemoglobin electrophoreses were normal. The last findings together with negative family histories and the onset of the anemia during adulthood serve to exclude thalassemia. Each of the four patients who had leukemic bone marrow manifested changes of myelomonocytic leukemia or its preleukemic phase:[10,11] bizarre megaloblastoid erythropoiesis, abnormal granulopoiesis with an overabundance of blasts and progranulocytes, and normal to increased numbers of atypical megakaryocytes. Three patients responded to pharmacologic doses of pyridoxine with a substantial rise in their hemoglobin levels to near normal; the remaining two patients exhibited reticulocytosis and a decrease in transfusion requirements, but their hemoglobin concentrations changed only moderately. Three of the five patients have subsequently died from diseases unrelated to their hematologic problems. Two patients are still alive; one has relapsed and is requiring additional therapeutic measures for her refractory anemia. Case 3 has a hemoglobin level of 13.7 gm/100 but continues to exhibit qualitative abnormalities in the peripheral blood and preleukemic changes in the bone marrow.

If suboptimal hematologic response is accepted as one of the diagnostic criteria, many "sideroblastic anemias" can be designated "pyridoxine-responsive anemias." The marked variations in presentation and response to pyridoxine attest to the heterogeneity of this group of anemias.[2,4,9,12] We believe that responsiveness to pharmacologic doses of pyridoxine may, in some cases, be characteristic of leukemia. Each of our patients with leukemia had erythrocytic abnormalities with megaloblast-like or megaloblastoid features in the face of normal serum vitamin B_{12} or folate levels or unresponsiveness to the administration of these

agents. Therefore, one wonders if certain of the reports of patients with pyridoxine-responsive anemia and "megaloblastic" morphology were not examples of neoplastic changes.

Recent studies of the pyridoxine-responsive anemias point to one, and possibly two, enzymatic defects in hemoglobin synthesis.[12,15] In the formation of delta-aminolevulinic acid from succinate and glycine, the enzyme aminolevulinic acid synthetase, which requires pyridoxine as a cofactor, has been found to be defective (Figure 5). There is suggestive evidence in this group of patients that heme synthetase, which is needed for the linking of iron and protoporphyrin to form heme, also functions abnormally. However, these observations do not detract from the possibility that the basic disorder may be leukemic, for many enzymatic defects have been associated with malignant processes.

The red cell enzymatic defects in the pyridoxine-responsive anemias may result from iron overload.[12,14] These enzymes are located in the mitochondria where iron accumulation could inhibit their activity, and when excess iron is reduced by phlebotomy, enzyme function more closely approaches normal. However, it is difficult to know which is the primary mechanism. Does iron overload cause or is it in turn caused by enzyme abnormalities? Because three of our five patients with pyridoxine-responsive anemia had leukemic bone marrows and a fourth had changes of an evolving myeloproliferative process, we believe a neoplastic change to be the primary factor in these cases with iron overload and enzymatic defects both resulting therefrom. Such a concept lends support to the malignant potentiality of the primary sideroblastic anemias.[16]

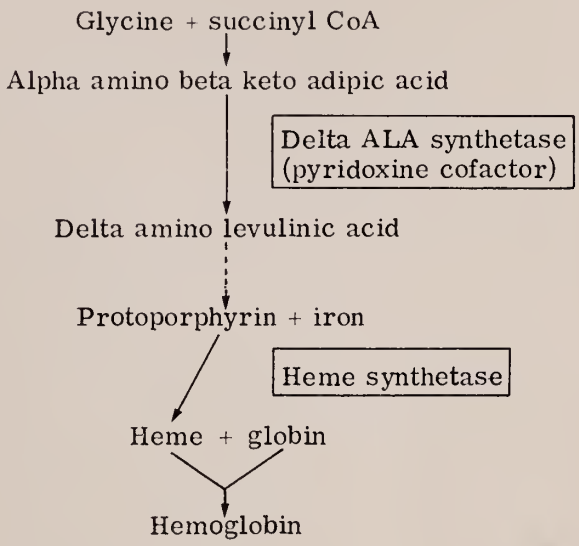


Fig. 5—Site of action of two enzymes which may be defective in pyridoxine-responsive anemias; figure shows route of protoporphyrin and hemoglobin synthesis.

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Be friendly with the folks you know . . . if it weren't for them, you'd be a total stranger.

Referred Pain to the Ear

EUGENE B. KERN, M.D.

EAR PAIN or otalgia caused by an acute inflammation of the middle or external ear is often easily diagnosed on physical examination. The symptom of earache, however, can be caused by disorders which arise distant from the ear in question. When the origin of pain is remote from the area of the disease process, it is called referred pain. Patients complaining of otalgia in whom no obvious evidence of ear disease can be found must be examined for lesions other than those associated with the ear. Inflammatory or malignant lesions of the nasopharynx, base of the tongue, or larynx may cause referred pain to the ear and must therefore be excluded.

When a patient has an earache, particularly a mild one, he usually can indicate only that the pain is in a general area of the external ear. The patient should be asked to localize the specific site of the pain because some patients misinterpret what is meant by ear pain and point to the temporomandibular joint, angle of the mandible, or the region of the temporal artery, thereby providing the examiner with an important clue as to the cause of the pain. When the source of the ear pain cannot be found on examination of the ear, the sites from which the referred pain may arise must be considered (Table and Figure).

The fifth, seventh, ninth, and 10th cranial nerves have sensory fibers in the regions of the auricle, the external auditory canal, tympanic membrane, and middle ear. There is considerable overlap in the distribution of these sensory fibers. Also, the second and third cervical nerves supply sensation to the postauricular region, while the auriculotemporal branch of the fifth nerve innervates a large region in front of the auricle of the external ear and around the temporomandibular joint. Usually, when examining a patient who has an earache but no inflammation in his middle or external ear, one cannot determine the precise sensory nerve distribution that the pain is being referred through until a lesion has been found. It is imperative before looking further that the external auditory canal be examined carefully so as not to overlook some small lesion (for example, furuncle or cancer).

Fifth Cranial Nerve (Trigeminal)

Dental disease may cause earache referred through the fifth cranial nerve (trigeminal). Molar impaction and infection are perhaps the most common causes of referred ear pain. Sinus inflammation in an antrum or in a posterior ethmoid or tumors in these areas may cause referred otalgia through the fifth cranial nerve, although this is

TABLE
Sensory Distribution Accounting for Referred Pain to the Ear

- Fifth cranial nerve (trigeminal nerve, mandibular division)
  - Oral cavity and floor of mouth
  - Teeth (lower)
  - Palate
  - Tongue (anterior two thirds)
  - Mandible (lower)
  - Temporomandibular joint
  - Preauricular region
  - Anterior tympanic membrane
- Seventh cranial nerve (facial nerve)
  - External auditory canal
  - Postauricular region
  - Middle ear (?)
- Ninth cranial nerve (glossopharyngeal nerve)
  - Tonsil
  - Base of tongue (posterior one third)
  - Nasopharynx
  - Eustachian tube
  - Pharynx (throat)
  - Middle ear
  - Mastoid air cells
  - Posterior tympanic membrane
  - External auditory canal
  - Postauricular region
- Tenth cranial nerve (vagus nerve)
  - Hypopharynx (throat)
  - Larynx
  - Trachea
  - Posterior tympanic membrane
  - External auditory canal
  - Postauricular region
- Cervical nerves (C-2 and C-3)
  - Postauricular region
  - Skin over mastoid region
  - Skin over anterior neck and thyroid region (suprahyoid and infrahyoid regions)

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.
See editorial, page 913.

probably rare. Acute or chronic disturbances of the temporomandibular joint may produce ear pain that is referred through the auriculotemporal branch of the fifth cranial nerve.

Seventh Cranial Nerve (Facial)

The seventh cranial nerve (facial) can cause otalgia principally in herpetic eruptions from viral infection of the geniculate ganglion. The pain is transient and often is overshadowed by other manifestations, particularly by the seventh-nerve palsy. Other lesions could touch the sensory branches of the facial nerve and produce otalgia; however, this is probably uncommon.

Ninth Cranial Nerve (Glossopharyngeal)

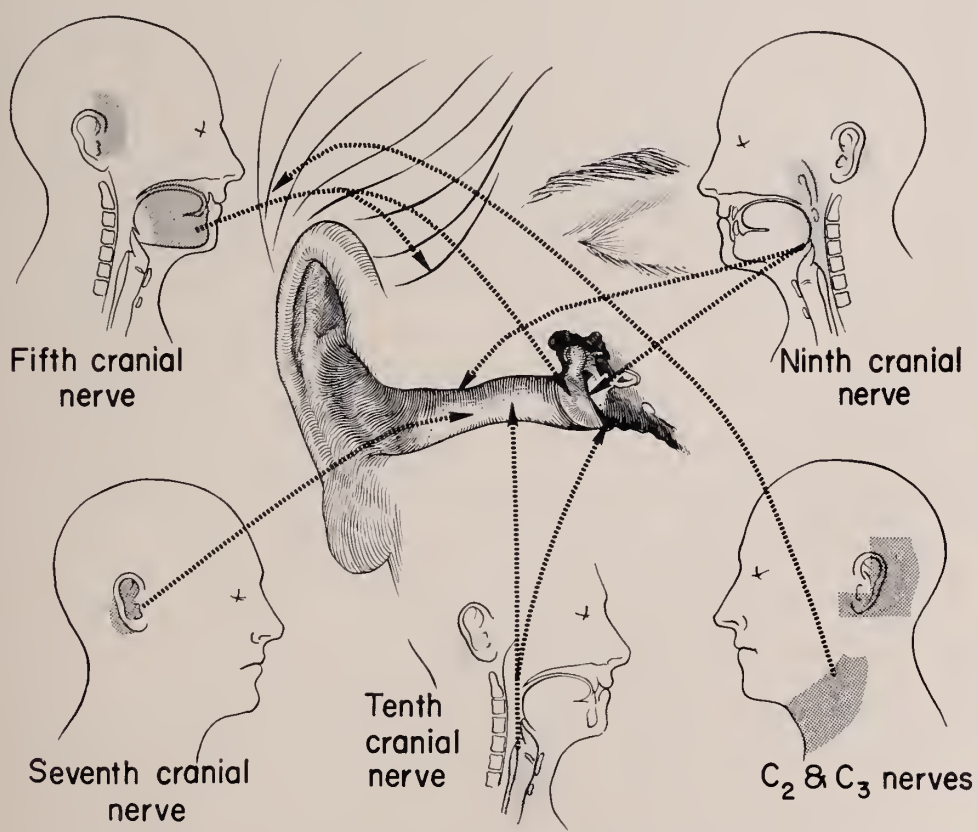
A lesion in the distribution of the ninth cranial nerve (glossopharyngeal), the nasopharynx, eustachian tube, the region of the palatine tonsils, adjacent base of the tongue, or the lingual tonsils, may cause earache by way of the glossopharyngeal nerve. The inflammatory process of this region usually accounts for the earache that may occur in the early convalescence from tonsillectomy. Afflictions of the ninth cranial nerve, such as glossopharyngeal tic, also may cause earache. The pain and discomfort of glossopharyngeal tic is sharp, short, and lance-like and can be precipitated either by drinking a cold liquid or by swallowing.

Tenth Cranial Nerve (Vagus)

A patient with an inflammatory or neoplastic lesion in the epiglottis of the larynx, in the pyriform sinus (hypopharynx), or in the trachea often complains of earache on the involved side. The reference is through the superior laryngeal branch of the vagus nerve, the 10th cranial nerve. Frequently, a patient with this problem also complains of hoarseness. This symptom allows the examiner to direct his attention to the region that is producing referred pain to the ear.

Cervical Plexus (C-2 and C-3)

The second and third cervical nerves also are pathways for referred pain to the external ear and the soft tissues in the mastoid process; inflammation or mass lesions of the thyroid may produce re-



Figure—Diagram of pathways from various sensory distributions accounting for referred pain to the ear.

ferred pain to the ear. Otalgia may be an early manifestation of thyroid carcinoma especially in children. Pain is mediated by C-2 and C-3 through the cervical plexus to the auricle. The upper cervical nerve roots supply the postauricular region. Pain due to their irritation, for example, cervical spondylosis or sternocleidomastoid myalgia, may be referred to the ear or mastoid process. There is also the possibility that otalgia may be due to an autonomic imbalance along the course of blood vessels related to these parts.

Summary

Pain may be referred to the ear from sensory fibers of the fifth, seventh, ninth, or 10th cranial nerves or from the cervical plexus (C-2 and C-3). If the patient can point to the painful site, this is an important clue to the cause. If the source of the pain is not readily determined from the examination of the external ear, tympanic membrane, or preauricular and postauricular regions, then distant sites must be examined because the pain may be the result of an occult malignancy. These distant sites involve the sensory distribution of the fifth, seventh, ninth, and 10th cranial nerves and the second and third cervical nerves. Common sources of this referred pain are the oral cavity (teeth, tongue, tonsil), temporomandibular joint, nasopharynx, and perilaryngeal regions.

Request for Physican's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers has received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the Association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Because of limitation of space, pictures oriented horizontally are preferred. All pictures will be returned if identified with the name and address of the physician. Please submit your pictures as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 375 Jackson St., St. Paul, Minnesota 55101.

Farrell Stiegler, M.D.
Cover Editor

Honorary Doctoral Degree

An honorary doctoral degree from the University of Munich, Germany, was recently bestowed on Cecil J. Watson, M.D. of Minneapolis for his important research contribution to medical science. The degree was awarded in conjunction with the 500th anniversary of the University.

Dr. Watson is the past head of the department of medicine at the school of medicine at the University of Minnesota and is presently the senior consultant to the University's medical unit at Abbott-Northwestern Hospital.

He was the only American among the seven physicians so honored.

In 1930-32 Dr. Watson was a resident physician at the University of Munich where he studied under Nobel Prize Winner, Dr. Hans Fischer, who, until his death, was a world authority on bile pigments and hemoglobin metabolism. Since then Dr. Watson has become a leading authority in the study and treatment of liver diseases and in the study of bile pigments and porphyrins and it has been in these areas where he has conducted significant medical research.

Management of Gastrojejunal Ulcer

A Review of 106 Cases

DAVID D. DuBOIS, M.D. AND OLIVER H. BEAHRS, M.D.

In recent years much knowledge about gastrojejunal ulcer disease has become available. For many years the frequency of recurrent gastrojejunal ulcers seemed to be one of the most important if not the only consideration in selecting the type of operation for duodenal ulcer. Recurrent peptic ulceration occurs after approximately 2% of operations for gastric ulcer and five to 10% of operations for duodenal ulcer. Of patients with recurrent peptic ulceration, 95% are those originally operated on for duodenal ulcer. Today factors other than recurrence are important in selecting the appropriate operation for peptic ulceration. These factors include maintenance of weight, degree of postprandial symptoms, diarrhea, and overall condition of the patient.

Gastrojejunal ulceration represents a surgical failure of the previous operation for peptic ulcer disease. Although some authors have reported limited success with the medical management of gastrojejunal ulcers, most favor surgical treatment of the ulcer once the diagnosis has been established: first, because the original ulcer was a surgical problem and, second, because the initial surgical treatment was unsuccessful.

The first operation performed for a gastrojejunal ulcer at the Mayo Clinic was in 1912. In 1948, Priestley and Gibson[1] reported results of a five- to 10-year follow-up of 103 patients who had had gastric resection for gastrojejunal ulcer; the ulcer had developed after gastroenterostomy had been carried out for a previous duodenal ulcer. Further surgical treatment was required in 5.8% of the patients because of secondary recurrent ulceration.

In 1960, Walters[2] reported a six- to 10-year follow-up study of patients who had gastrojejunal ulcer after gastroenterostomy. They found that gastric resection was superior to vagotomy in nine cases in which gastrojejunostomy had been performed initially and that vagotomy was more effective than re-resection of the stomach when the gastrojejunal ulcer developed after resection of a third to a half of the stomach at the first surgery.

In 1966 Wychulis et al.[3] reported the experience with 360 patients who were operated on for recurrent gastrojejunal ulcer between the years 1950 and 1960. The average interval between the initial operation and the symptoms of recurrent ulceration was 7.4 years after gastroenterostomy, 1.9 years after gastric resection, 1.7 years after gastroenterostomy and vagotomy, and 1.1 years after gastric resection and vagotomy. Surgical treatment varied according to the type of initial operation and the surgical findings. Average follow-up data of 7.9 years on 305 patients indicated that the results were excellent or very good in 259 (84.9%), unsatisfactory in 31 (10.2%), and poor in 15 (4.9%).

Our Series

Our series is comprised of 106 patients who were treated at the Mayo Clinic for gastrojejunal ulcer from 1961 through 1965. Included are those patients who had their second operation done at our clinic for peptic ulcer during this period. There was a minimum follow-up period of five years for all 106 patients.

The 106 patients included in the series had a surgically or roentgenographically demonstrable gastrojejunal ulcer.

Findings and Comment

Age

The average age of the 106 patients was 54.2 years, with a range of approximately 24 years.

Sex

Men outnumbered women by approximately four to one: 84 (79%) men to 22 (21%) women.

Location of the original ulcers

Ninety-two (87%) of the patients originally

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

had duodenal ulcers, six (6%) had gastric ulcers, and one (1%) had a combination of a duodenal and gastric ulcer. In seven patients, the location of the original ulcer was unknown.

Roentgenographic Findings

Of the 106 patients who underwent surgical procedures for gastrojejunal ulcer, 75 patients had preoperative Xrays of the upper gastrointestinal tract, 59 (78.6%) of these 75 had evidence of gastrojejunal ulcer on roentgenograms. This group included all patients whether their ulcer was on the gastric side, on the jejunal side of the anastomosis, or in the stoma. Ulcer could not be demonstrated by roentgenogram in 16 (21.4%). There was no record of roentgenograms having been done for 31 patients. The percentage of positive results (78.6%) by roentgen examination in our series is somewhat higher than that recorded by other authors. Although x-ray examination is less often an aid in diagnosing gastrojejunal ulcers than in diagnosing gastric or duodenal ulcers, the results are positive in more than 50% of the cases, and thus the x-ray examination has been worthwhile.

Gastric Acidity

Of the 106 patients, 53 had free acid before their second surgery, 16 patients did not, and 37 patients either had no determinations done or the results had not been recorded.

Time Interval to Recurrence after First Operation

Thirty patients who underwent gastroenterostomy had symptoms of recurrent ulcer an average of 152 months after operation, compared to 56 patients with Billroth II who had symptoms of recurrent ulcer an average of only 31 months postoperatively. The recurrence time was even less for patients who had vagotomy as part of the original procedure. For those who had vagotomy and gastroenterostomy initially, the average recurrence time was 43 months, compared to those who had Billroth II and vagotomy, for whom the recurrence was six months. However, there were only five patients in this group. For the 99 patients in whom the time interval was known, the average was 67.8 months between the initial surgery and the recurrence of ulcer symptoms.

Nature of Recurrent Symptoms after First Operation

Ninety-nine patients had one or more symptoms; 79 had recurrent epigastric pain, 50 had recurrent gastrointestinal bleeding, 26 had clinical evidence of gastrointestinal obstruction, five had symptoms related to a fistula, and seven had symptoms not clearly stated in the history.

Distribution of Patients and Average Months Between First and Second Operations

When gastroenterostomy was the initial operation, a Billroth II was the procedure most often done for the recurrence; next in frequency was a Billroth II with vagotomy. When Billroth II was the initial procedure, a gastric re-resection employing a Billroth II anastomosis with vagotomy was the most frequent second procedure; a gastric re-resection (Billroth II) was next frequent, and an abdominal vagotomy was third. Of all the procedures used for a second operation, the gastric re-resection with the Billroth II anastomosis and vagotomy and the gastric re-resection (Billroth II) were used equally often (22 cases). A gastric re-resection (Billroth II) was used in 17 cases, and abdominal vagotomy was used in 16 cases. Twenty-nine had procedures of another type.

Postoperative Course after Operation for Recurrent Ulcer

After the second operation, 82 patients had uneventful postoperative courses, two had recurrent gastrointestinal bleeding, one had obstruction, and 21 had miscellaneous complications; several patients had more than one complication.

Ulcer Condition after Surgery for Recurrent Ulcer

Of the 106 patients, 86 completed the part of the follow-up questionnaire that concerned the general effect of the second operation: 80 (93% of these) reported improvement and six (7%) noted no improvement. Because of the few patients in each surgical group, the percentage of improvement for each respective surgical procedure was not statistically significant. Of 81 patients who reported their health status, 57 (70%) said it was good or excellent and six (7%) said it was poor. Of 89 who reported regarding ulcers, 72 (81%) said that they had had no recurrence of ulcer symptoms, and 17 (19%) had had recurrence of one or more ulcer symptoms. Among the 17 patients with symptoms, eight had pain, four had vomiting, four had diarrhea, six had bleeding, and four had symptoms of another nature. An attempt was made to establish whether the recurrent symptoms were due to recurrent ulcer, the previous surgery, combined effect, or other causes. However, the evaluation was not valid or reliable enough to test for statistical significance.

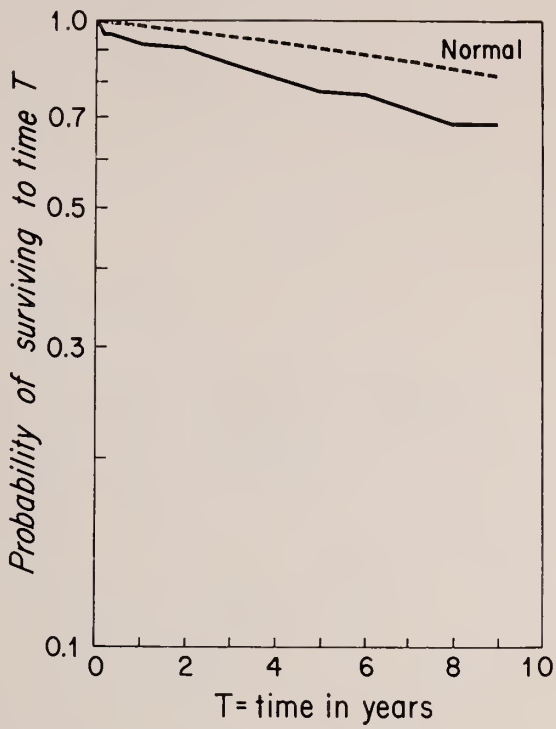
For the 17 patients with symptoms, the average time from the second operation to the occurrence of the symptoms was 29 months, with a range

rom six months (Billroth I and vagotomy) to 61 nonths (gastric re-resection or Billroth II).

Seven of 87 patients (8%) each required a hird operation for peptic ulcer disease: two of 1 patients whose second operation was gastric e-resection (Billroth II) and vagotomy, two of 12 vho had had a Billroth II procedure, one of 15 vho had had gastric re-resection (Billroth II), one of three who had had gastric re-resection (Billroth) and vagotomy, and one of nine who had had a Billroth II and vagotomy. Nineteen patients did not report regarding further procedures.

At the end of the follow-up period, 30 patients were dead. Deaths were attributable to various causes, the most common being cirrhosis of the iver in seven cases and arteriosclerotic heart disease in six cases.

The five-year survival rate for patients with recurrent ulcer was 78%. This compares with an expected five-year survival rate of 90% for a comparable normal population (Figure). At nine years, the rates were 69% and 82% respectively. The survival curves are shown in the Figure.



Figure—Survival after second ulcer operation. Solid line represents experience in this series, broken line experience in normal population without recurrent ulcer.

Conclusions and Summary

A series of 106 patients with gastrojejunal ulcer were operated on between 1961 and 1965 at the Mayo Clinic. Follow-up data were available on all patients. The most frequently used second procedures were gastric re-resection (Billroth II) with vagotomy (22 cases), gastric resection (Billroth II) (22 cases), gastric re-resection (Billroth II) (17 cases), and abdominal vagotomy (16 cases). 24 patients had a procedure of another type. Fifty-seven of 81 patients who completed questionnaires (70%) reported that their health was good or excellent after the second operation. Eighty of the 86 patients (93%) noted improvement in their condition. Seven of 87 (8%) required a third surgical treatment. Secondary surgery for gastrojejunal ulcer following surgical treatment of duodenal or gastric ulcer must be tailored to fit the current pathological findings. The second operation is dictated also in part by the type of procedure done at the initial surgery. Generalizations cannot be made and the best surgical judgment has to be used based on the experience of the operating surgeon. The five-year survival rate for patients with recurrent ulcer disease was 78% compared to 90% in a comparable normal population group. The most common cause of death was cirrhosis of the liver.

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1. Priestley JT and Gibson RH: Gastrojejunal ulcer: clinical features and late results. Arch Surg 56:625, 1948.
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3. Wychulis AR, Priestley JT and Foulk WT: A study of 360 patients with gastrojejunal ulceration. Surg Gynecol Obstet 122:89, 1966.

An empty stomach is not a good political adviser.—Albert Einstein.

Minnesota Medical Information Service

A new and exciting "on-line" information service is available free to Minnesota physicians. Called the Minnesota Medical Information Service (MMIS), the project is funded by Northlands Regional Medical Program and housed at the University of Minnesota.

Any Minnesota physician may call the information service 24 hours a day via a single toll-free telephone number given below.

Information Services Available

1. *Medical Library Service*—If a physician needs information from the current medical literature, he will be connected to a trained librarian at the University of Minnesota Bio-Medical Library. After learning the topic on which information is needed, the librarian will conduct a fast, on-line literature search using *MEDLINE,* a computer link to the National Library of Medicine in Washington. She will then describe the ten or so most recent articles published on the subject requested, make photocopies requested from the journals in the Bio-Medical Library, and have them in the mail to the physician the same day. The standard photocopy charge of ten cents per page will be imposed, plus one dollar for handling. There will be no charge to the physician for the literature search. This service is not meant to replace existing medical library services, but to provide such services if the librarian in the local hospital cannot do the search or does not have the journal requested. We hope, through this service, to serve the practicing doctors' information needs quickly and efficiently.

2. *Medical/Dental Specialty Advice*—If a physician has a clinical problem he needs help with, he may call MMIS and state his problem. MMIS maintains a list of specialists from the University full-time and clinical faculty, and the Mayo Clinic, and will have the next specialist "on call" return the call to the requesting physician promptly to provide that specialist-practitioner dialogue on demand. As with the library service, we do not wish to disturb any existing consultant relationships, only to provide help for a practitioner when he does not know who to call about a specific clinical problem.

3. *Dial Access Tapes*—Northlands Regional Medical Program has maintained a dial access tape service for years, connected to the University of Wisconsin. We have now moved the tape library to the University of Minnesota and provide these short (five minute) audio learning sessions on over 500 clinical topics. These are kept up to date and listed in a catalogue available from Mr. LeRoy Berglund, Northlands Regional Medical Program, 375 Jackson Street, St. Paul 55101. Simply give the MMIS operator the tape number you would like to hear, sit back and listen.

4. *Drug Information Service*—The Drug Information Center (DIC) is staffed by pharmacists from 8 a.m. to 5 p.m. Monday through Friday. During evening, night and weekend hours the health science students, who will be answering the MMIS telephones, will handle all calls to the DIC. If necessary, they will be assisted by an on-call pharmacist.

Types of questions that you may wish to direct to the DIC include the following:

1. Drug identification and availability—i.e. commercially available U.S. drugs, foreign drug products, and investigational drugs.
2. Therapeutic uses or doses for new and old drugs.
3. Therapeutic compatibility—i.e. drug interactions.
4. Pharmaceutical compatibility—i.e. I.V. incompatibilities.
5. Reports of side effects, contraindication and adverse reactions.
6. Biopharmaceutical information.

Calls regarding poison information should be directed to your nearest poison control center.

In summary, MMIS is designed to provide the practicing physician with medical information through audio tapes, through dialogue with specialists, through access to articles in the medical literature, and through drug information. All these services are available 24 hours a day to all physicians in Minnesota.

The telephone numbers to call are: *373-1855* for Minneapolis-St. Paul area, *1-800-552-7210* (toll free) for outstate area.

Winston R. Miller, M.D.
Director, Northlands Regional Medical Program

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*.

*Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

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IN EDEMA*—IN HYPERTENSION*

If you've seen one, have you really seen them all?

The following patient profiles represent typical clinical situations, but do not necessarily represent actual cases.

Age 22, previously normal me
with occasional menorrhagia
on a sequential O.C. for four m
Complains of heavy flow
occasional intracyclic bleedin
edema, tender swollen breast
Indicates estrogen excess
1st choice: Switch to a com
bination 50-mcg.-estrogen O C
(such as **Demulen**®).

Age 19, small breasts, minor hirsutism, oily hair and skin. History of metrorrhagia, skipped or scanty menses. New user.
Indicates androgenic excess or estrogen deficiency (fertility is suspect).
1st choice: An estrogen-dominant O.C. (such as **Enovid-E**®).

Age 25, average frame, poor complexion. No problem with menses, normal para 1. On a low-estrogen/high-progestogen O.C. for two years. Now complains of scanty flow, decreased libido, depression.
Indicates probable buildup of progestogen-related side effects.
1st choice: Switch to a center-spectrum O.C. with more estrogen, less progestational activity (such as **Ovulen**®).

Age 21, short, mammose, with normal menses, some acne. Was put on prenuptial regimen of 50-mcg.-estrogen/moderate-progestogen O.C. for two months. Now has increased acne.
Indicates metabolic production of androgen or relative estrogen deficiency
1st choice: Switch to a 100-mcg.-estrogen combination (such as **Enovid-E**® or a sequential).



Unmasked, physiologically and anatomically, they're not all the same. A basic difference lies in their hormone profiles. One may secrete too much estrogen, another not enough...or perhaps too much androgen; the vast majority would fit somewhere into the broad center spectrum.

Although the profiles described below may not be completely predictive, in optimal O.C. selection, the estrogen-progestogen activity ratio should be carefully matched to the patient profile. Searle offers you O.C.s in a range not only suitable for your patients in the balanced center spectrum, but also adaptable to the patient with another type of hormone profile.

Oral contraceptives are complex medications. Among the commonly reported adverse reactions are: intracycle bleeding, fluid retention, tender or swollen breasts, exacerbation of acne condition, changes in libido, amenorrhea while on medication and upon discontinuance, nausea, leg cramps, headaches, weight gain. Therefore, after reference to the prescribing information, oral contraceptives should be prescribed with care.

*Note: In some patients any level of exogenous estrogen or progestogen may produce symptoms of excess hormone activity.

, tall, slender, athletic,
at chest. On a progestogen-
ant 50-mcg.-estrogen O.C.
current trichomoniasis
onilia.
cales estrogen deficiency and
s of progestogen in current O.C.
choice: Switch to a com-
on pill with 100 mcg.
en and less progestational
y (such as **Enovid-E**® or
n or a sequential).

Age 23, "Miss America" figure, previously normal menses, healthy skin and hair. On a 50-mcg.-estrogen pill for four months. Complains of intracyclic bleeding.
Indicates probable need for more estrogen.
1st choice: Switch to a center-spectrum O.C. with more estrogen and moderate progestogen dominance (such as **Ovulen**®).

Age 21, college senior, average build. On highly progestogen-dominant/low-dose-estrogen O.C. for six months. Now complains of amenorrhea, between-cycle headaches, weight gain.
Indicates probable progestogen excess.
1st choice: Switch to a center-spectrum pill (such as **Ovulen**®).

Age 27, slightly overweight, multiparous. Nausea with all three pregnancies and with a sequential O.C. three years ago. Has pre-menstrual fluid retention and leg cramps.
Indicates probable excess of estrogen.
1st choice: A 50-mcg.-estrogen/progestogen-dominant pill (such as **Demulen**®).



Ovulen® a balanced center-spectrum O.C. for most

Each white tablet contains ethynodiol diacetate 1 mg./mestranol 0.1 mg.

Demulen® a moderately progestogen-dominant O.C. for many

Each white tablet contains ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg.

Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

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Enovid-E® a moderately estrogen-dominant O.C. for some

Each tablet contains norethynodrel 2.5 mg./mestranol 0.1 mg.

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a brief summary
prescribing information,
ease see next page.

a family of O.C. products to help you match the right pill to the right patient

Ovulen®

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Demulen®

Each white tablet contains
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Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

Actions – Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note – Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication – Ovulen and Demulen are indicated for oral contraception.

Contraindications – Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings – The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4 4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions – The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any pos influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adr hepatic or uterine function awaits further study. A decrease in glucose toler has been observed in a significant percentage of patients on oral contra tives. The mechanism of this decrease is obscure. For this reason, diabet tients should be carefully observed while receiving Ovulen or Demulen the The age of the patient constitutes no absolute limiting factor, although treatn with Ovulen or Demulen may mask the onset of the climacteric. The patho should be advised of Ovulen or Demulen therapy when relevant specimens submitted. Susceptible women may experience an increase in blood pres following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives – A statistically significant association has been demonstrated betw use of oral contraceptives and the following serious adverse reactions: thron phlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relat ship has been neither confirmed nor refuted for the following serious adve reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abd inal cramps and bloating), breakthrough bleeding, spotting, change in menst flow, amenorrhea during and after treatment, edema, chloasma or melas breast changes (tenderness, enlargement and secretion), change in we (increase or decrease), changes in cervical erosion and cervical secretions, s pression of lactation when given immediately post partum, cholestatic jaund migraine, rash (allergic), rise in blood pressure in susceptible individuals i mental depression.

Although the following adverse reactions have been reported in users oral contraceptives, an association has been neither confirmed nor refut anovulation post treatment, premenstrual-like syndrome, changes in libi changes in appetite, cystitis-like syndrome, headache, nervousness, d ness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforr erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral cont ceptives: hepatic function: increased sulfobromophthalein retention and oth tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and thyroid function: increase in PBI and butanol extractable protein bound iodi and decrease in T^3 uptake values; metyrapone test and pregnanediol det mination.

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Editorials

Mayo Medical School: "What's Past Is Prologue"

EARLY IN THE YEAR 1968, the staff of the Division of Education, Mayo Foundation, was charged by the Trustees of Mayo Foundation to prepare a model of a medical school in the Mayo institutional setting. This model was presented to the Board in July. There followed four months of intensive analysis and discussion in which a host of committees and individual members of our staff were involved. Each departmental chairman was requested to submit to the Board of Trustees a report on the viewpoint of his departmental members with respect to the medical school. At the meeting of the Trustees on November 25, the Trustees received the reports of the departmental chairmen, of the Board of Governors of Mayo Clinic, and of the Commission of University Presidents, an advisory council developed jointly under the auspices of the Regents of the University of Minnesota and the Trustees of Mayo Foundation. The Trustees then took the following actions:

Resolved, That the Board of Trustees favors the development of undergraduate medical education as a part of the activities of Mayo Foundation. This development is to be conditioned upon its financing, with minor exceptions, by funds to be raised from public and private sources not now part of Mayo Foundation's income and capital flow.

Resolved further, That there be an exploration in depth of a suitable academic affiliation, with reasonable autonomy, for the Mayo Medical School, or alternatively, of its independence as a recognized degree granting institution.

During 1969 discussion proceeded with the University of Minnesota on extension of our affiliation agreement to include a Mayo medical school. On March 13, 1970, the Regents of the University and the Trustees of Mayo Foundation entered into such an affiliation. I shall quote five paragraphs from the section of the agreement entitled "General Principles of Affiliation":

I. The University of Minnesota through its College of Medical Sciences and Mayo Foundation are the two senior and major Minnesota institutions in the field of medical service, medical education and medical research. As such, they bear a heavy and shared leadership responsibility to the State of Minnesota and to a substantial region beyond the boundaries of the State in the important area of health.

II. The University is a public institution established by the Constitution of the State, enjoying a preponderance of public with a measure of private support. Mayo Foundation, including its proposed medical school, exists as a private trust for public purposes enjoying a preponderance of private but a measure of public support. Each institution identifies its public character by vesting ultimate authority and responsibility in Regents or Trustees, respectively, so selected as to insure appropriate representation of the public.

III. There is envisioned an equal partnership of responsible, mature, independent institutions, capable (granted vision, foresight, and mutual understanding) of a synergistic combination of strengths not now wholly congruent.

IV. There is mutual recognition of the irreducible residuals of institutional independence, embedded in the organic law of each, which cannot be eliminated, but which need not be barriers to men of good will working for the public good.

V. The two institutions agree to build upon the mutually profitable association of more than fifty years in graduate medical education. The aim is an ever broader, more fruitful collaboration.

Mayo Medical School thus functions as an educational unit of the University of Minnesota owned and operated by Mayo Foundation. Its dean is nominated by the Trustees of Mayo Foundation to



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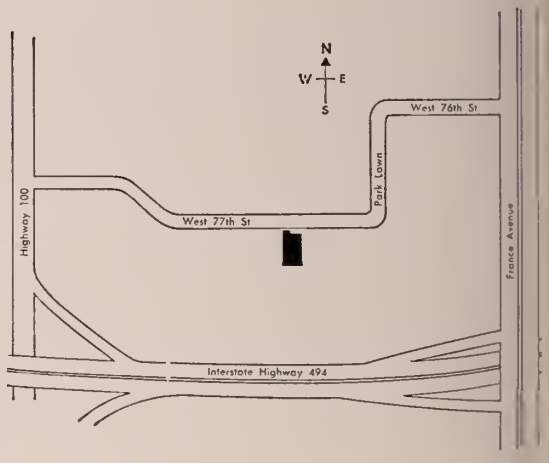
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he President of the University of Minnesota and s Regents. Its students will be granted their M.D. degree on recommendation of the Faculty nd Dean of Mayo Medical School to the Univerity President and Regents. Mayo Graduate School of Medicine will continue to be a part of he Graduate School of the University of Minneota.

To foster application of the general principles enumerated in the Affiliation Agreement, a University of Minnesota-Mayo Foundation Liaison Committee was established. That Committee is composed of representatives from the Board of Regents of the University and the Board of Trustees, Mayo Foundation, as well as two senior administrative officers of each institution.

With the academic affiliation agreed on, we were able to concentrate on other aspects of planning for the school. We faced major tasks in designing curriculum, developing faculty, and raising money to pay for our proposed programs. We have attempted to design a curriculum based on established institutional strengths as these are represented in faculty, facilities, and institutional traditions and goals. We have been determined to maintain "one house." If Mayo Medical School is to fulfill the high purposes envisioned for it, then it must be an expression of the finest resources and purposes of the existing Mayo institutions, not a new and foreign program standing discrete and apart from all that has gone before and proceeds today. We believe we have set up an academic program which reflects these clearly defined purposes. Moreover, we shall continue to recruit our staff and faculty as always we have: to total institutional purposes. We shall not have a faculty specific to "the medical school."

As regards payment of the costs, the Commission of University Presidents had advised that when we could see our way through the first 10 years of operation, we should proceed. We calculated as carefully as we could the *incremental* costs of an undergraduate educational program in the Mayo setting. These summated to 33 million dollars, over 80% of which figure is in support of faculty time and overhead on that time. We turned to three principal sources for enlistment of this financial support. These were as follows:

We requested of the state of Minnesota capitation support of our students at the rate of $8,000 per student per year. The 1971 session of the Minnesota Legislature approved this support of Minnesota residents only for the biennium beginning July 1, 1971. We have indicated to the legislators that continuation of support at this level is essential to the stable fiscal operation of Mayo Medical School.

We worked with other institutions and commissions in fostering federal legislation designed to increase markedly the support of undergraduate medical education. Legislation authorizing substantial increase in federal support, primarily on a capitation basis, was enacted by the Congress. Unfortunately, corresponding appropriations approximated only 65%. Bringing appropriations to the level of authorizations is an objective for fiscal year 1973 and worthy of broad support from the medical profession.

Through the Mayo Development Program initiated in 1965, we approached private sources of philanthropy—foundations, corporations, and private donors—and they have responded generously. We achieved our goal of securing (from these private donors) something in excess of one third of our anticipated costs of operating the medical school for its initial 10 years.

On November 12, 1971, the Board of Trustees of Mayo Foundation authorized opening Mayo Medical School in September 1972. Forty students compose the first class, 90% of whom will be residents of Minnesota. We sought to identify and recruit students of diverse talents and professional goals for that first class, as we shall for succeeding classes, and we shall foster that diversity through curricular design, student counselling, and preceptorial assignments. As funds from our Development Program increase, we shall take a larger proportion of our students from states other than Minnesota, probably by increasing total size of the class and not by reducing the number of Minnesotans appointed.

Faculty to execute the curriculum has been selected from among our clinical and research staff. During this first curricular year, we shall try to facilitate the student's transition from the formal academic programs of his college education into an environment of learning wherein one day he will come to realize that the patient is his greatest teacher. From the beginning, we shall seek to foster patterns of behavior which will permit the student to garner data efficiently from diverse sources and by various means—above all else, from the patient himself. These patterns, once established, will serve him well through that



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lifelong process of professional growth and learning to which he must devote himself if he is to serve his patients well and provide them the finest medical care. We believe our institutional resources are well adapted to this academic mission.

We embark today on a new and challenging journey. But we intend that this altered course shall fault no old commitment nor sacrifice worthy traditions long revered.

We proceed into these new responsibilities in such humility of spirit as becomes our inexperience. But we are sustained by that confidence which belongs to those who have met past challenges and have overcome.

Mayo Medical School, Rochester, Minnesota.

Raymond D. Pruitt, M.D.
Dean

The University of Minnesota Welcomes the Mayo Medical School

The opening of the Mayo Medical School runs current with a time in which health is one of our most pressing national issues. The people of America are becoming increasingly aware of health care as a basic human right. The traditional health care delivery system of the country has been quite a good one in past years. However, it is now being required to exercise a new ingenuity in order to cope with changing patterns of population distribution which have left some population groups, such as those in rural and urban areas, relatively isolated from adequate medical services.

In order to overcome some of these problems, the academic community with the help of organized professional groups, have recognized that there are at least three major components which require particular focus. First, *enough* of all kinds of health professionals must be trained. Then there must be the development of innovative health care delivery programs that effectively utilize the skills of health professionals and which make use of modern technology for efficiency, while maintaining a strong humanistic element for the comfort of the patient. It is not enough to develop new programs. The programs must be evaluated and properly accredited to maintain standards, and they must merit the acceptance of both professionals and patients they involve. Finally we need supportive research programs which probe and attempt to solve difficult health problems which plague the population.

Minnesota health practitioners and health institutions have been responsive in all three of these areas. They are internationally known for specialized medical care, for training programs and basic research, and some have provided national leadership in the exploration of alternative health care systems. Our state legislators, who consistently have desired a high level of health for their people, have encouraged and supported these efforts.

Although Minnesota has as few problems in the area of health as any state, we have shared a problem common to many other states: that pertaining to the distribution and types of services offered by medical professionals—i.e., the need for greater availability of primary care.

The University of Minnesota is working hard to help increase primary medical care where it is needed in the State. Twin Cities Medical School admissions have increased from 162 in 1969 to 239 in 1973. In addition each year approximately 30 students transfer from the Universities of North and South Dakota for their junior and senior years. Additionally about 24 students will enter the new two year medical program in Duluth beginning this academic year.

Another major step which directs itself to the challenge of primary care in Minnesota is the development of the undergraduate medical education program at the new Mayo Medical School, the curriculum of which places an emphasis on primary practice.

On March 13, 1970, at a meeting of the University Regents and the Mayo Board of Trustees, Chairman of the Mayo Board of Governors Dr. Emmerson Ward and University President Malcolm Moos signed an affiliation agreement for Mayo Medical School. This act added another dimension to an affiliation between the two institutions which has been in effect since 1915.

The existence of the Mayo Medical School especially complements the traditionally outstanding work of the Mayo Clinic and is a strong demonstration of the sensitivity of those of the Mayo complex to the health needs of the State. The new School will admit 40 students this year (36 of whom are residents of Minnesota). This means that by the mid 70's, the medical schools of Minnesota will graduate over 325 students per year!

It gives me great pleasure to offer best wishes and to pledge the support and cooperation of the University of Minnesota Health Sciences to Mayo Medical School. Furthermore, we all join in congratulations to Dr. Ward; to Mr. Atherton Bean, Chairman of the Mayo Board of Trustees; to Dr. Raymond Pruitt, Dean of the Mayo Medical School; and to the distinguished faculty and all other supporters of the School. We heartily welcome the establishment of another fine medical school for Minnesota.

Lyle A. French, M.D.
Vice President for Health Sciences Affairs
University of Minnesota

The Mayo Medical School

THIS ISSUE OF MINNESOTA MEDICINE is devoted to an event of great significance in Minnesota, the opening of the Mayo Medical School in Rochester. At the turn of the century several medical schools existed in the state but these were all absorbed into the University before 1910. For some six decades then there was only one.

Now there are two and soon three with the opening of the Duluth school. There can be no question that all are urgently needed; all graduates of Minnesota schools will immediately find full employment for their needed skills.

Rochester with the Mayo Clinic is the natural choice for a medical school. Its faculty, both in clinical medicine and in basic science, matches that of the great schools throughout the country.

As Lyle French points out, the several schools in Minnesota will work together with the University of Minnesota co-ordinating all. The Mayo Medical School will enhance the name of its founders, of Rochester and the State. The world of medicine will know the impact of this significant event. We look forward to the contributions that will be made by the graduates of the new school in Rochester. The contributors to this issue, guest edited by Raymond Pruitt, Dean of the Mayo Medical School, are all members of his faculty. We thank them not only for the October issue but also for their massive support to this journal in previous contributions. We confidently expect the pages of MINNESOTA MEDICINE in the future will expose some of the work of this institution, and undoubtedly, manuscripts of graduates of the new medical school.

Reuben Berman, M.D.
Editor

Dr. Henry Stanley Plummer

THE MEDICAL PROFESSION is indebted to Henry Plummer on many scores. His contributions to our knowledge of thyroid disease are well known and widely appreciated. Of comparable importance was his early work concerning esophageal disease and the management of difficult esophageal problems, particularly stricture.

Perhaps Henry Plummer's most notable and lasting contributions were his remarkably innovative approaches to the effective organization of medical practice. His appreciation that the physical layout of a building and the development of a proper record system could materially affect the quality and effectiveness of medical practice was nearly unique in his time. The group practice of medicine, which continues to grow in importance, is deeply indebted to his early insights.

Keys* has given us a graphic picture of the genius of Henry Plummer and has told us of his great human warmth. It is timely that Dr. Keys has reminded us once again of this fine clinician, this imaginative organizer, this "medical Thomas Jefferson" of whom Minnesota can be so justly proud.

Robert B. Howard, M.D.
Minneapolis, Minnesota

*See page 955.

Is Dementia Treatable?

One in ten Americans is 65 years old or more. With more elderly in our midst, stereotypes of the aged as enfeebled, helpless, and infirm must come under our increasing purview if we are to avoid the gerontophobic conclusion that old age itself is a disease. It is not, but it may be accompanied by various disorders such as dementia. As Sandok* noted in this issue, some forms of dementia are definitely treatable, leading to an improvement in the quality of life experienced. In the functional disorders, for example, the value of psychotherapy for some of the elderly is not to be underestimated,[1] medication and electroshock therapy also proving quite useful and desirable. Clinical approaches to dementia must also include paying attention to those emotionally involved with the elderly, such as relatives whose ability to cope may be strengthened by family conference and other measures. Not everyone who appears demented is elderly. Facing the problem of dementia, treatable and untreatable, may not only challenge diagnostic acumen, but also ripen the ethical and philosophical fruits of practice.

Murray S. Locke, M.D.
Minneapolis, Minnesota

*See page 878.

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Referred Otalgia

Harold Wolff stated in his classical treatise on head pain that "the ear is unique in that there is no structure in the body of comparable size that is supplied by sensory nerves from so many neural segments."[4] The ear receives sensory fibers from cranial nerves five, seven, nine, and ten and from cervical roots two and three. The ear may be the site of referred pain resulting from pathologic states in areas remote from it.

There is some variation in the contributions of the individual nerves. In addition a number of investigators have demonstrated overlap in the central connections of the nerves supplying the ear in the brain stem and cervical cord. For example stimulation of the upper cervical roots may result in pain experienced in the ear.[2] Consequently localization of the specific nerve involved in ear pain is very difficult.

Kern* has sharply etched the dilemma facing the physician whose examination of the patient with painful ear fails to disclose local pathology in the ear.[1] His discussion is quite helpful in detailing the more important conditions referring pain to the ear and the alternative sites to be checked. It is particularly important as Kern points out to search for occult malignancy in the nasopharynx and larynx. Dental disease often refers pain to the area of the ear and the initial dental evaluation may not disclose the source so that persistence may be required.

The fifth cranial nerve also supplies the intracranial dura and tentorium. Wirth and Van Buren have demonstrated pain referred to the ear from stimulation of the dura.[3] Intracranial malignant, inflammatory, and vascular processes must also be considered as causes of referred otalgia although precise localization of the source may not be possible.

John M. McKelvey, M.D.
Minneapolis, Minnesota

*See page 896.

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Dr. O. T. Clagett, a Mayo Clinic surgeon, has been named 1972 winner of the Presidential Citation of the American College of Chest Physicians, one of the five highest honors given by the college. He will be honored at a convocation Oct. 23 in Denver for his "achievements in and contributions" to the field of chest surgery.



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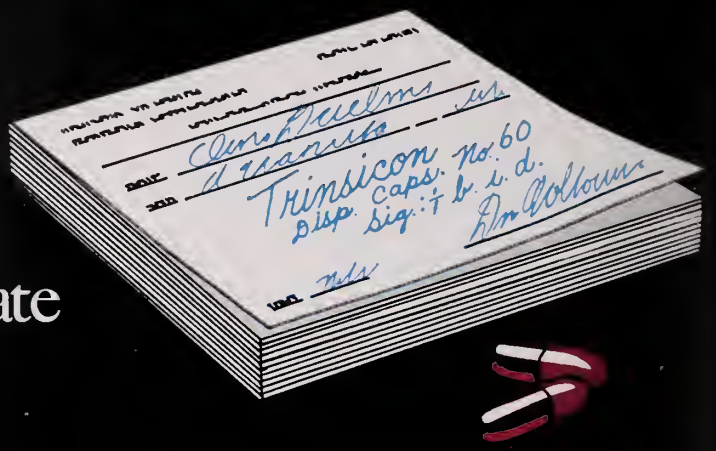
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Concentrates of intrinsic factor derived from hog gastric, pyloric, and duodenal mucosa have been used successfully in patients who lack intrinsic factor. For example, Fouts *et al.* maintained patients with pernicious anemia in clinical remission with oral therapy (liver extracts or intrinsic factor concentrate with vitamin B_{12}) for as long as twenty-nine years.

After total gastrectomy, Ficarra found multifactor preparations taken orally to be "just as effective in maintaining blood levels as any medication that has to be administered parenterally." His study was based on twenty-four patients who had survived for five years after total gastrectomy for cancer and who had been taking two Pulvules Trinsicon daily.

Folic Acid—Folic acid deficiency is the immediate cause of most, if not all, cases of nutritional megaloblastic anemia and of the megaloblastic anemias of pregnancy and infancy; usually, it is also at least partially responsible for the megaloblastic anemias of malabsorption syndromes, e.g., tropical and nontropical sprue.

It is apparent that in vitamin B_{12} deficiency (e.g., pernicious anemia), lack of this vitamin results in impaired utilization of folic acid. There are other evidences of the close folic acid-vitamin B_{12} interrelationship: (1) B_{12} influences the storage, absorption, and utilization of folic acid, and (2), as a deficiency of B_{12} progresses, the requirement for folic acid increases. However, folic acid does not change the requirement for vitamin B_{12}.

Iron—A very common anemia is that due to iron deficiency. In most cases, the response to iron salts is prompt, safe, and predictable. Within limits, the response is quicker and more certain to large doses of iron than to small doses.

Each Pulvule Trinsicon furnishes 110 mg. of elemental iron (as ferrous fumarate) to provide a maximum response.

Ascorbic Acid—Vitamin C plays a role in anemia therapy. It augments the conversion of folic acid to its active form, folinic acid. In addition, ascorbic acid promotes the reduction of ferric iron in food to the more readily absorbed ferrous form. Severe and prolonged vitamin C deficiency is associated with an anemia which is usually hypochromic but occasionally megaloblastic in type.

Contraindications and Precautions: Anemia is a manifestation that requires appropriate investigation to determine its cause or causes.

Folic acid *alone* is unwarranted in the treatment of pure vitamin-B_{12}-deficiency states, such as pernicious anemia. Indeed, the use of folic acid in large doses in pernicious anemia without adequate vitamin B_{12} may result in hematologic remission but neurological progression.

As with all preparations containing intrinsic factor, resistance may develop in some cases of pernicious anemia to the potentiation of absorption of physiological doses of vitamin B_{12}. If resistance occurs, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential and are recommended.

In extremely rare instances, skin rash suggesting allergy has been noted following the oral administration of liver-stomach material. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Hemochromatosis and hemosiderosis are contraindications to iron therapy.

Adverse Reactions: In rare instances, iron in therapeutic doses produces gastrointestinal reactions, such as diarrhea or constipation. Reducing the dose and administering it with meals will minimize these effects in the iron-sensitive patient.

Dosage: One Pulvule twice a day. (Two Pulvules daily produce a standard response in the average uncomplicated case of pernicious anemia.)

How Supplied: Pulvules Trinsicon® (hematinic concentrate with intrinsic factor, Lilly), in bottles of 60 and 500 and in Identi-Dose® (unit dose medication, Lilly) in boxes of 100.

[xxxx]

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Case Report

Werner's Syndrome
Case Report of A Variant

CLAYTON REYNOLDS, M.D., J. DESMOND, O'DUFFY, M.B., B.Ch. AND
W. MITCHELL SAMS, JR., M.D.

In 1904, WERNER[1] DESCRIBED four cases of a peculiar disorder he called "cataract in connection with scleroderma." Thirty years later, Oppenheimer and Kugel[2] reviewed his cases, added two new ones, and described the characteristics of the full syndrome as follows: (1) shortness of stature with characteristic habitus of thin extremities and normal trunk, (2) premature baldness, (3) premature graying of hair, (4) atrophy of skin beginning in the second decade, (5) acral skin ulcers, (6) juvenile cataracts, (7) hypogonadism, (8) tendency to mild diabetes mellitus, (9) calcification of blood vessels, (10) osteoporosis with periarticular calcification, and (11) tendency to occur in siblings.

We present here the history, physical findings, and laboratory data of a patient representing a variant of this syndrome in that the first three features were absent. The distinction between Werner's syndrome and progressive systemic sclerosis is emphasized.

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Report of Case

History

An unmarried 43-year-old man presented at the Mayo Clinic in October 1970 because of dysphagia and heartburn. He had been born in Ontario, Canada, to a 19-year-old mother of Scottish origin and a 21-year-old father of Irish descent. There was no known consanguinity and the family history, traced by the patient for four generations, was negative for cataracts and diabetes mellitus; graying of the hair and baldness began in one brother at age 25 years. Pregnancy and delivery were uneventful, and the patient was considered normal at birth. At age four years, bilateral nerve deafness followed whooping cough. A photograph taken at that time and examined by us showed no remarkable features but one at age six showed wrinkling of the face, especially around the mouth; this was the first evidence of abnormality.

The patient had a normal active childhood until, in his early teens, episodes of fever and arthritis in the knees, ankles, and elbows occurred. At age 16, he noted that the skin of his arms, fingers, and feet was tight and dry. Contractures of the fingers and toes resulted in ulcerations at bony prominences. Puberty did not occur; the genitalia remained small, pubic and axillary hair growth was scanty, and his voice was high-pitched. By the late teens, his eyes had become prominent, his nose



Fig. 1—Appearance of patient on admission. Proptosis, wrinkled perioral skin, sparse beard, and aphakic pupils.

pinched, and his face wrinkled, all combining to make him appear prematurely old.

His growth did not stop prematurely; in fact, he kept growing until age 25, at which time he first shaved. Over the ensuing years he attended the Toronto General Hospital for intensive rehabilitation and multiple surgical procedures. The first operation was at age 29 when he had bilateral cataract removal for decreasing vision and a tarsorrhaphy for proptosis. Ulcers of the feet required skin grafting, and the toe contractures were so severe that bilateral midtarsal amputation became necessary.

At age 39, amputation of the right third and fourth distal and middle phalanges and fusion of the right fifth proximal and distal interphalangeal joints were done to relieve flexion contractures. There was progressive tightening of the skin on the legs, arms, hands, and feet. Raynaud's phenomenon did not occur. During the prolonged hospital stay necessary for these procedures, numerous urinary tract infections occurred.

At age 41, flexion contractures of the right metacarpophalangeal joints were treated by the insertion of Silastic prostheses. Metabolic studies at that time revealed mild adult-type diabetes mellitus.

While in the hospital, he developed symptoms of



Fig. 2—Roentgenogram with barium, showing diaphragmatic hernia.

esophagitis and had a gastrointestinal hemorrhage requiring blood transfusion. A roentgenographic study with barium revealed a diaphragmatic hernia. His referral was prompted by a second major gastrointestinal hemorrhage in September 1970, with weight loss, dysphagia, and persistent esophagitis uncontrolled by antacids.

Physical Examination

The patient had the general appearance of an emaciated, wrinkle-faced man (Figure 1) who walked as if on stilts, because of previous midfoot amputations. His blood pressure was 130/70 mm Hg, pulse rate 76/min, weight 113 pounds, and height 70 inches. There was no loss or graying of the scalp hair. The skin around the mouth was wrinkled, the nose was pinched, and he was unable to open his mouth widely. His voice was child-like. He wore well-fitting upper dentures; the lower teeth were carious. Severe sensorineural hearing loss was partly corrected by a hearing aid. His eyes were prominent; the pupils were irregular and did not react to light. There were well-healed scars of lid surgery. Each cornea showed vascularized scarring inferiorly; on the left this had the appearance of a 4-mm pterygium. Funduscopic findings were normal. The thyroid appeared normal.

The skin of the lower extremities was thin, bound down, and sclerotic over bony prominences. Telangiectasia was not present. Over the trunk the skin exhibited a mottled, reticular hypopigmentation but with normal texture. There was marked hyperpigmentation of the coccygeal and ischial tuberosities. Both anterior thighs and calves showed scars from graft donor sites. No synovitis was noted.

The thin extremities contrasted sharply with the normal-sized trunk. Elbow and finger contractures were present. Range of motion of all joints of the extremities was limited; for example, the knees could be flexed only 70° and the metacarpophalangeal joints, only 45°. The right third and fourth middle and distal phalanges were missing.

There was no gynecomastia. Pubic and axillary hair were absent. The penis was small; the left testicle was absent and the right was atrophic, and the prostate was small. Markedly atrophic, but not myotonic, muscles were found in all extremities. The patient was cooperative, of normal intelligence, and able to carry out all usual activities of self-care. Results of cardiovascular and abdominal examinations were normal except for mild hepatomegaly and slight epigastric tenderness to deep palpation. Temporal, occipital, femoral, and popliteal pulsations were normal. The posterior tibial arteries were not felt, perhaps because the tightness and induration of the skin obscured their pulsations.

Laboratory Data

Routine. The following were normal or negative: electrocardiogram, hemoglobin concentration, leukocyte total and differential counts, platelet count, stool for occult blood, serum iron, serum uric acid, urine specific gravity, and urine sugar. The urine showed mild proteinuria (2+), one leukocyte and two erythrocytes per high-power field, and an occasional hyaline cast. Blood urea was slightly increased, 56 mg/100 ml (normal, 17 to 51). Creatinine clearance was diminished to 55 ml/min/1.73

n² (normal, 120 to 130). The erythrocyte sedimentation ate was 60 mm in one hour (Westergren).

Hematologic Studies. A peripheral blood smear showed nacrocytosis suggestive of vitamin B_{12} or folate deficiency; the serum B_{12} level was 238 pg/ml (normal, 60 to 850), and serum folate was 1.4 ng/ml (normal, to 16).

Metabolic Studies: The urinary screen for amino acids nd homogentisic acid was normal. Serum lipids were: holesterol, 332 mg/100 ml (normal, 150 to 300); triglycerides, 99 mg/100 ml (normal, <150); and phospholipids, 321 mg/100 ml (normal, 180 to 320). The ollowing were normal or negative: serum calcium, phosphorus, and alkaline phosphatase, buccal smear for Barr odies, karyotype, fasting and two-hour postprandial lood glucose, serum thyroxine, ^{131}I uptake, thyroid scan, serum luteinizing hormone, and response to ACTH stimulation. The 24-hour urinary excretion of 17-ketogenic steroids was 9.2 mg (normal, four to 14), of 17-ketosteroids 3.2 mg (normal, six to 21), and of pituitary gonadotropin six rat units (normal, four to 20); plasma testosterone was 64 ng/100 ml (normal, 250 to 1,200).

Immunologic Studies. Plasma proteins were: albumin, 3.8 gm/100 ml; α_1-globulin, 0.56; α_2-globulin, 2.1; β-globulin, 1.1; and γ-globulin, 1.0. The LE cell, rheumatoid factor, VDRL serologic, antinuclear antibody, and antithyroid antibody tests were negative.

Gastrointestinal Studies. Esophageal motility was normal. Results of gastric juice analysis (12-hour specimen) were: volume, 275 ml; pH 2.0; titratable acid, 91 mEq/liter; and output, 7.5 mEq/hr. Liver function tests gave the following data: prothrombin time, 18 seconds (normal, 17 to 19); sulfobromophthalein retention, 0% in 45 minutes (normal, <5%); serum glutamic-oxaloacetic transaminase, 22 units/liter (normal, <24); serum lactic dehydrogenase, 77 units/liter (normal, <127); and serum creatine phosphokinase, 28 units/liter (normal, <71).

Roentgenographic Studies. Roentgenograms of the extremities showed marked loss of soft tissue, osteoporosis with old bilateral metacarpal fractures, metacarpophalangeal joint prostheses in the third, fourth, and fifth digits of the right hand, and contracture deformity of both hands. The abdominal aorta and pelvic arteries were calcified. The upper gastrointestinal series (Figure 2) revealed a short esophagus with diaphragmatic hernia and evidence of gastroesophageal reflux. The chest and head were normal.

Skin Biopsy

Histological examination (Figure 3 *left*) showed atrophic skin. The epidermis showed moderate flattening of the rete ridges with hyperkeratosis. In sections stained with hematoxylin and eosin, the hair follicles and sweat glands were normal in appearance and number for the skin of the arm. The collagen fibers were fine and frayed. There were blue-stained fibers intermixed between the collagen fibers, particularly in the upper portion of the dermis. Elastic tissue stains revealed a marked increase in thick and clumped elastic fibers in the upper third of the dermis. The elastic fibers in the deeper dermis appeared normal. All of these findings are those of actinic or solar elastosis resulting from chronic sun exposure in

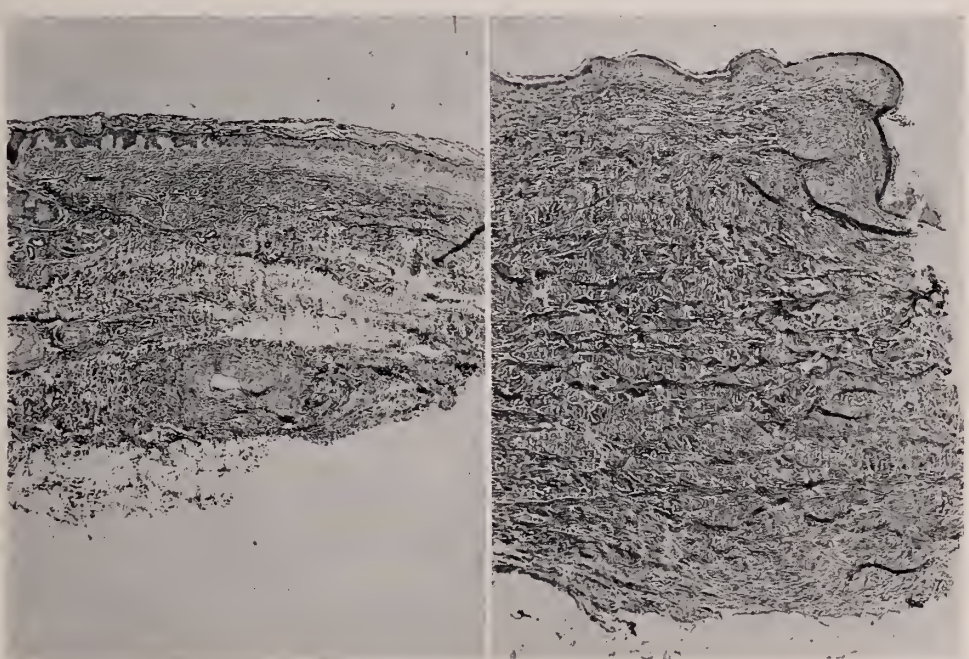


Fig. 3—Skin biopsies. (Hematoxylin and eosin; x 35.) *Left,* From forearm of our patient, showing atrophy of dermis with normal appendages. *Right,* From forearm of patient with typical case of scleroderma, showing thickening of dermis with atrophy of appendages.

an individual of fair complexion.

A skin biopsy from a similar site in a typical case of scleroderma (Figure 3 *right*) showed a marked decrease in appendageal structures, particularly hair follicles and sweat glands. The sweat glands that remained were small and located within the mid-dermis rather than in the lower dermis as is usual. The entire dermis was greatly thickened for this part of the body, and the individual collagen fibers were thickened, had a homogeneous appearance, and had lost much of their striations.

A quick-frozen biopsy specimen from our patient, sectioned on a cryostat and stained with fluorescein-conjugated anti-human immunoglobulins, failed to demonstrate in vivo fixed antibodies for basement membrane, intercellular space, or blood vessels.

Hospital Course

Two esophageal dilatations resulted in relief of the dysphagia but worsening of the esophagitis. Because the latter was uncontrolled by full doses of antacids, the patient underwent repair of the hiatal hernia. The surgical procedure included a transabdominal vagotomy, pyloroplasty, and repair of the sliding esophageal hiatal hernia combined with a Nissen fundoplication and posterior gastropexy. An episode of postoperative atelectasis with retention of tracheobronchial secretions responded to conservative measures. Staphylococcal sep cemia developed but responded to large doses antibiotics. Bilateral keratitis due to incomple closures of lids during sleep was considerably in proved by blepharorrhaphy. He was dismissed the 21st postoperative day with no esophage symptoms.

Discussion

The differential diagnosis included Werner syndrome (heredofamilial dermatosis with sk ulcers), Rothmund's syndrome (heredofamilial de matosis with telangiectasia), scleroderma (pr gressive systemic sclerosis), and the Hutchinso Gilford syndrome. The Table lists the features Werner's syndrome, the present case, and Rotl mund's syndrome.

We suggest this case is a variant of Werner syndrome. Evidence for there being *form frustes* of this disease has in the past centered o the findings of diabetes mellitus[3] and prematu graying of the hair[4] in relatives of patients wit the fully developed syndrome. Until the preci etiology or biochemical lesion can be establishe patients with minor variations from the full syr drome may be regarded as having the basic di ease. The facial features in this case, as well a the areas of skin involved in the atrophic proces are strikingly similar to those in a case reporte by Shelby and Vaughn[5] as juvenile Werner's syr drome. Those authors pointed out that moder

TABLE
Contrastng Features of Werner's Syndrome, Present Case, and Rothmund's Syndrome

Features	Werner's	Present case	Rothmund's
Familial occurrence	Present	Absent	Absent
Skin changes	Tightening, hyperkeratosis, atrophy of skin & subcutaneous tissue: ulcers of extremities; no telangiectasis	Same	Venous distention & telangiectasis with pigmentation; no tightening or hyperkeratosis
Age, onset of skin changes	20-30 yr	6 yr	Few months
Trophic ulcers	Prominent	Prominent	Absent
Muscular development	Poor, atrophic	Poor, atrophic	Better
Cataracts	Early adult life	20 yr	Early childhood
Vocal cords	Epithelial changes	Not examined	Normal
Sexual deve'opment	Absent	Absent	Normal
Hair	Premature graying, baldness	Normal	Normal
Short stature	Present	Absent	Absent
Arteriosclerosis	Prominent	Present, not prominent	Absent
Osteoporosis	Prominent	Prominent	Absent
Diabetes mellitus	Often present	Present	Absent
Thyroid dysfunction	Variably present	Absent	Absent
Proptosis	Present	Present	Absent
Soft-tissue calcification	Present	Present	Absent

drugs and treatment may alter the findings and course of a disease, thus changing it from its classic description. This comment applies to our patient who has had prolonged and intensive medical care in the form of ophthalmic, orthopedic, and gastric surgery, antibiotics, and hormones.

Scleroderma

Scleroderma (progressive systemic sclerosis) is excluded for many reasons. In this disease the skin on the face is thick and bound down and loses its wrinkles. In our patient, the skin was atrophic with increased wrinkling, a finding completely out of keeping with scleroderma. Histologically, the two are distinct. In our patient there was no fibrosis or sclerosis of collagen fibers but there was loss of rete pegs and papillary projections and fragmentation of elastic tissue which was decreased in amount. The use of the term "scleroderma-like" should be discouraged; it is unfortunate that Werner used it in his original description[1] and writers have continued to use it even after the publication of Thannhauser's review.[6]

Although childhood scleroderma is rare, it does occur and persist into adulthood. The absence of Raynaud's phenomenon and of esophageal motility abnormality strongly contradicts the diagnosis of progressive systemic sclerosis, especially after so many years of skin involvement. The difficult problem of an esophageal hernia with severe reflux esophagitis presented by this patient has not previously been reported in connection with Werner's syndrome. The absence of a motility abnormality in the esophagus makes it unlikely that shortening of the esophagus by a sclerodermatous process is responsible. Possibly, the short esophagus is a congenital abnormality; its appearance in this patient may be a chance occurrence.

Rothmund's Syndrome

Rothmund's syndrome is excluded in this case by the fact that the skin lesions did not develop in the first few months of life, ulcerations appeared, and the skin was mostly involved over the distal extremities. Telangiectasia, a prominent feature of Rothmund's syndrome, was not present, but atrophy and tautness of the skin were. Atrophy of extremities, osteoporosis, diabetes, and arteriosclerosis are not found in Rothmund's syndrome but were present in our case. The age at which cataracts were first noted is more in keeping with Werner's than with Rothmund's syndrome.

Because our patient presented with skin ulcers and cataracts, this case does not fit the description of the Hutchinson-Gilford syndrome. In addition, the evidence of premature aging did not develop in our patient at as early an age.

Hypogonadism

The hypogonadism in this patient has features of both of the usual categories of hypergonadotropism and hypogonadotropism, since the urinary excretion of pituitary FSH was low normal in association with an atrophic testicle on one side and no testicle on the other. One would expect high urinary gonadotropin excretion in primary testicular failure. The best evidence of gonadal failure is not the 24-hour urinary 17-ketosteroid value, which can be accounted for on the basis of chronic debilitation, but the low level of plasma testosterone.

In diseases in which the etiology is established, as in homocystinuria,[7] the clinical picture need not be uniform from one patient to another in order to make the diagnosis. If multiple defects are responsible for Werner's syndrome, it would be even more likely that features would be variable. Variability in inheritance is recognized as sporadic cases have been reported.[8] Our case may be a sporadic one, the only evidence of a familial tendency being early graying and baldness in an older brother.

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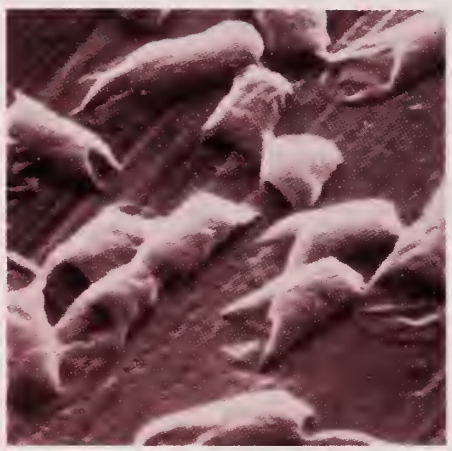
*In suspected or documented gram-negative sepsis due to susceptible organisms, GARAMYCIN Injectable may be considered as initial therapy. The decision to continue therapy with this drug should be based on the results of susceptibility tests, the severity of the infection, and the important concepts contained in the Warning Box below.

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Proven clinical efficacy[1,4-13]

GARAMYCIN Injectable may be lifesaving in septicemia . . . may give a dramatic response in wounds and burns complicated by sepsis. GARAMYCIN Injectable has also demonstrated outstanding results in serious gram-negative infections other than sepsis, such as serious respiratory infections and selected urinary tract infections. To date, GARAMYCIN Injectable has been the subject of more than 1,500 published papers and 12 international symposia.





Note: The photomicrographs of gram-negative organisms reproduced here were obtained by a relatively new process employing a scanning beam electron microscope. The pathogens represented are *Klebsiella pneumoniae, Escherichia coli,* and *Proteus mirabilis.* The colors shown here are an artist's representation. The magnification is 10,000X.



WARNING: Patients treated wit GARAMYCIN Injectable should be d close clinical observation because t potential toxicity associated with e use of this drug.

Ototoxicity, both vestibular an auditory, can occur in patients, p those with pre-existing renal dam e treated with GARAMYCIN Injectal , usually for longer periods or with hi doses than recommended.

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A high degree of sensitivity maintained[14-16]

Bacterial resistance to GARAMYCIN Injectable has not been a problem to date. In the laboratory, resistance has been demonstrated to develop slowly in stepwise fashion. No one-step mutations to high resistance have been reported. One investigator noted: "In the experience so far with [gentamicin], which is 7 or 8 years, in centers where it's been restricted to parenteral use, resistance has not appreciably changed."[14] Another authority "...found very little emergence of resistance" during eight years of use.[15]

In a survey of published studies on resistance to gentamicin, Weinstein and co-workers[16] report little change in bacterial sensitivity since 1963 in the percentage of sensitive strains. *In vitro* sensitivity was determined in all cases by the tube-dilution method.



Relatively low incidence of adverse reactions[3,14,17]

As with certain other aminoglycoside antibiotics, ototoxicity (primarily vestibular with gentamicin) and potential nephrotoxicity are risks of therapy.

Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy.

In contrast to kanamycin, neomycin, and streptomycin, which primarily cause deafness or difficulties in the auditory end organs of the eighth nerve, gentamicin primarily causes labyrinthian dysfunction.[14] This dysfunction, manifested by dizziness (not deafness) has, in most cases, been transitory.

As to nephrotoxicity, according to Finland,[3] "as in the case of kanamycin, the nephrotoxicity was found to be largely 'potential,' and very little if any has been encountered except with obviously excessive doses or in patients with already damaged kidneys."

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rotoxic, and this should be kept in l when it is used in patients with xisting renal impairment.
onitoring of renal and eighth nerve tion is recommended during therapy itients with known impairment of l function. This testing is also mmended in patients with normal l function at onset of therapy who lop evidence of nitrogen retention easing BUN, NPN, creatinine or ria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

Usage in Pregnancy: Safety for use in pregnancy has not been established.

See Clinical Considerations section which follows...

When preculture signs point to gram-negative sepsis...

Garamycin® Injectable
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Each cc. contains gentamicin sulfate equivalent to 40 mg. gentamicin
For Parenteral Administration

WARNING: Patients treated with GARAMYCIN Injectable should be under close clinical observation because of the potential toxicity associated with the use of this drug.

Ototoxicity, both vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment.

Monitoring of renal and eighth nerve function is recommended during therapy of patients with known impairment of renal function. This testing is also recommended in patients with normal renal function at onset of therapy who develop evidence of nitrogen retention (increasing BUN, NPN, creatinine or oliguria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause toxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

USAGE IN PREGNANCY Safety for use in pregnancy has not been established.

INDICATIONS GARAMYCIN Injectable is indicated, with due regard for relative toxicity of antibiotics, in the treatment of serious infections caused by susceptible strains of the following microorganisms:

Pseudomonas aeruginosa, Proteus species (indole-positive and indole-negative), **Escherichia coli** and **Klebsiella-Enterobacter-Serratia** species.

Clinical studies have shown GARAMYCIN Injectable to be effective in septicemia and serious infections of the central nervous system (meningitis), urinary tract, respiratory tract, gastrointestinal tract, skin and soft tissue (including burns).

Bacteriologic tests to determine the causative organisms and their susceptibility to gentamicin should be performed.

Bacterial resistance to gentamicin develops slowly in stepwise fashion; there have been no one-step mutations to high resistance.

In suspected or documented gram-negative sepsis, GARAMYCIN may be considered as initial therapy. The decision to continue therapy with this drug should be based on the results of susceptibility tests, the severity of the infection, and the important additional concepts contained in the "Warning Box." In the neonate with suspected sepsis or staphylococcal pneumonia, a penicillin type drug is usually indicated as concomitant antimicrobial therapy.

GARAMYCIN Injectable has been shown to be effective in serious staphylococcal infections. It may be considered in those infections when penicillins or other less potentially toxic drugs are contraindicated and bacterial susceptibility testing and clinical judgment indicate its use.

CONTRAINDICATIONS A history of hypersensitivity to gentamicin is a contraindication to its use.

WARNINGS (See "Warning Box.")

PRECAUTIONS Neuromuscular blockade and respiratory paralysis have been reported in the cat receiving high doses (40 mg./kg.) of gentamicin. The possibility of these phenomena occurring in man should be considered if gentamicin is administered to patients receiving neuromuscular blocking agents such as succinylcholine and tubocurarine.

Treatment with gentamicin may result in overgrowth of nonsusceptible organisms. If this occurs, appropriate therapy is indicated.

ADVERSE REACTIONS

Nephrotoxicity: Adverse renal effects, as demonstrated by rising BUN, NPN, serum creatinine and oliguria, have been reported. They occur more frequently in patients with a history of renal impairment treated with larger than recommended dosage.

Neurotoxicity: Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss.

Numbness, skin tingling, muscle twitching, and convulsions have also been reported.

Note: The risk of toxic reactions is low in patients with normal renal function who do not receive GARAMYCIN Injectable at higher doses or for longer periods of time than recommended.

Other reported adverse reactions, possibly related to gentamicin, include increased serum transaminase (SGOT, SGPT), increased serum bilirubin, transient hepatomegaly, decreased serum calcium; splenomegaly, anemia, increased and decreased reticulocyte counts, granulocytopenia, thrombocytopenia, purpura; fever, rash, itching, urticaria, generalized burning, joint pain, laryngeal edema; nausea, vomiting, headache, increased salivation, lethargy and decreased appetite, weight loss, pulmonary fibrosis, hypotension and hypertension.

DOSAGE AND ADMINISTRATION GARAMYCIN Injectable may be given intramuscularly or intravenously.

For Intramuscular Administration:

PATIENTS WITH NORMAL RENAL FUNCTION*

Adults: The recommended dosage for GARAMYCIN Injectable for patients with serious infections and normal renal function is 3 mg./kg./day, administered in three equal doses every 8 hours.

For patients weighing over 60 kg. (132 lb.), the usual dosage is 120 mg. (2 cc.) three times daily. For patients weighing 60 kg. (132 lb.) or less, the usual dose is 60 mg. (1.5 cc.) three times daily.

In patients with life-threatening infections, dosages up to 5 mg./kg./day may be administered in three or four equal doses. This dosage should be reduced to 3 mg./kg./day as soon as clinically indicated.

*In children and infants, the newborn, and patients with impaired renal function, dosage must be adjusted in accordance with instructions set forth in the Package Insert.

For Intravenous Administration:

The intravenous administration of GARAMYCIN Injectable is recommended in those circumstances when the intramuscular route is not available (e.g., patients in shock, with hematologic disorders, with severe burns or with reduced muscle mass).

For intravenous administration, in adults, a single dose of GARAMYCIN Injectable may be diluted in 100 or 200 cc. of sterile normal saline or a sterile solution of dextrose 5% in water; in infants and children the volume of diluent should be less. The concentration of gentamicin in solution, in both instances should normally not exceed 1 mg./cc. (0.1%). The solution is infused over a period of 1 to 2 hours.

The recommended dose for intravenous administration is identical to that recommended for intramuscular use.

GARAMYCIN Injectable should not be physically pre-mixed with other drugs, but should be administered separately in accordance with the recommended route of administration and dosage schedule.

HOW SUPPLIED GARAMYCIN Injectable, 40 mg. per cc., 2 cc. multiple dose vials for parenteral administration.

Also available, GARAMYCIN Pediatric Injectable, 10 mg. per cc., cc multiple-dose vials for parenteral administration.

APRIL, 197

AHFS Category 8:28

For more complete prescribing details, consult Package Insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Professional Services Department, Schering Corporation, Kenilworth, New Jersey 07033.

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Special Article

The Eye and Adverse Drug Effects

Some Selected Considerations

DENNIS M. ROBERTSON, M.D.

Numerous drugs have been implicated as causes of adverse reactions of the eye. In many instances reports of toxic reactions are isolated testimonials for which the likelihood of a cause-and-effect relationship is remote. In other instances undesirable side effects have been definitely established and can be linked directly to a specific drug. Whereas some side effects are serious, occasionally leading to permanent visual impairment or prompting emergency surgical treatment, others are relatively minor and accordingly generate little concern. While physicians may be aware of many of the ocular side effects induced by certain systemic drugs, the nonophthalmologist may be unaware of some of the serious systemic effects induced by topical ophthalmic preparations. It is important for the physician to recognize, for instance, not only that chloroquine may cause progressive pigmentary degeneration of the retina and blindness but also that certain topical antiglaucoma medications may decrease blood cholinesterases, a factor of concern when succinylcholine is considered with general anesthesia (anesthetic deaths have been noted in three cases in which topical diisofluorophosphate was used to treat glaucoma).[1]

This report reviews some selected considerations of toxicology of drugs as they relate to the eye. In general each drug will be considered relative to its local effect on the eye, its general effects from systemic absorption through the conjunctiva, and its adverse ocular effects when used systemically. A comprehensive review may be found in Grant's book, "Toxicology of the Eye."[2]

Drugs Which May Adversely Affect Intraocular Tension

Anticholinergic Drugs (Cycloplegics and Mydriatics)

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.
Presented in part at the meeting of the Minnesota State Medical Association, Rochester, May 18, 1972.

Topical-Local Effect.—The topical use of mydriatics or cycloplegics can precipitate acute angle-closure glaucoma in predisposed eyes. Such eyes generally have shallow anterior chambers and narrow entrance angles and may show a sharp increase in intraocular tension if the iris crowds the angle and interferes with aqueous outflow. Eyes that have a tendency to develop angle-closure glaucoma may be suspect if gross examination utilizing a light directed across the iris suggests an unusually shallow anterior chamber. Most eyes, however, may be dilated with little concern because angle-closure provocation is uncommon.

In contrast with eyes predisposed to narrow-angle glaucoma, in some patients with open-angle glaucoma, topical cycloplegics (cyclopentolate, atropine, homatropine, and scopolamine) can cause a significant transient increase in intraocular pressure (greater than six mm). This effect is unassociated with angle closure and rarely requires specific treatment. The response is apparently related to an influence on the ciliary body. In one study,[3] 23% of the patients in whom 1% cyclopentolate was instilled topically were noted to have such a pressure increase. The effect was not seen with 10% phenylephrine, ½% tropicamide, or 5% eucatropine.

Prolonged topical use of atropine has been occasionally associated with local hypersensitivity reactions such as chemosis and lid edema.

Topical-Systemic Effects.—The parasympatholytic agents, when applied topically (atropine, homatropine, scopolamine, and cyclopentolate), may cause systemic anticholinergic intoxication with central nervous system symptoms; these include visual hallucinations, restlessness, ataxia, delusion, stupor, and coma. The symptoms, although generally dose-related, may appear as an idiosyncratic response also. In either situation, symptoms usually can be reversed by the use of 1 mg of physostigmine given intramuscularly, intra-

venously, or subcutaneously.[4,5]

Systemic Anticholinergic Drugs.—The United States Food and Drug Administration requires that all drugs with anticholinergic effects be accompanied by a warning against their use in patients with glaucoma, even though published evidence has been insufficient to establish whether these warnings are justified.[6]

Several clinical studies, both short-term and long-term, have been done to determine whether anticholinergic agents elevate intraocular pressure by pupillary dilation or by changes in aqueous dynamics.[7-10] One clinical experiment designed to study possible short-term effects on intraocular pressure by a systemically administered proprietary drug containing belladonna alkaloids showed that the drug did not produce adverse effects on intraocular tension or pupil size. The study included both normal volunteers and patients with glaucoma.[7] Lazenby et al.[9] studied the long-term effects of systemic atropine (0.6 mg twice a day for seven days) in patients with glaucoma. They noted little change in intraocular pressure unless the eyes were positive responders to topically applied cyclopentolate.

Because most parasympatholytic agents do not cause pupillary dilation when given systemically, angle-closure glaucoma would not be expected to be precipitated. Actually, few systemic drugs directly cause pupillary dilation, with the exception of scopolamine[11] and possibly *L*-dopa.[12] Most other drugs reported to cause mydriasis do so indirectly through central nervous system stimulation (marihuana, for example).[2]

Although the repeated administration of anticholinergic medications should be used cautiously in open-angle glaucoma, only a few patients will have significant adverse effects. Furthermore, patients with narrow angles or shallow anterior chambers do not present an inordinate risk.[10] Weekly tonometric evaluation during the first few weeks of systemic administration appears to be a practical method for determining possible adverse effects. If no pressure increase is noted at the end of this period, the drug probably could be continued indefinitely with little concern about ocular complications.

Agents Used in Anesthesia

Succinylcholine.—Succinylcholine administered intravenously can cause a precipitous increase in intraocular pressure by stimulating the extraocular muscles mediated via the tonic neuromuscular system. Accordingly, its use when eye is open can promote disastrous consequenc and is contraindicated under such conditions. A ditionally, succinylcholine can relax ocular accor modation secondary to relaxation of the cilia muscle.[13]

Halothane.—Anesthesia with halothane m produce a significant decrease in intraocular pr sure. This is an important consideration in t selection of an anesthetic during procedures d signed to determine the presence of congenit glaucoma in young children, because a spurio normal reading induced by halothane might le to an unnecessary delay in implementing therapy A review of 1,835 cases in which halotha anesthesia was used primarily in children reve l a decrease in intraocular tensions that was b lieved to be secondary to a decrease in bloo pressure.[15]

Ketamine.—In a series of patients who we six months to 77 years old, ketamine hydrochl ride administered intravenously produced an ave age increase of four mm Hg in intraocul tension.[16] Although ketamine is useful for certai ophthalmic procedures,[17] its short duration (ap proximately eight minutes) and its tendency t cause nystagmus and involuntary motor move ments near the beginning and again at the end o the anesthetic time are hazardous factors in i selection as an anesthetic agent.

Drugs Used to Treat Glaucoma

As a part of any presurgical medical evaluation the physician must determine whether a patient i receiving any topical ophthalmic treatment fo glaucoma; this is important because glaucom therapy ordinarily should continue uninterrupte during the preoperative and postoperative period Many patients will not volunteer this information and the physician must then ask specifically whether the patient is using eye medications.

Topical

Miotics.—Common symptoms of all miotics in clude brow and eye ache (related to ciliary spasm and blurring of vision, particularly in the presby opic or prepresbyopic patient. Some of the miotic have caused cysts at the pupillary margin of th iris; these cysts, which are most frequently see with the cholinesterase inhibitors, are generally reversible and may be prevented by adding phenyl ephrine to the solution.[2,18] Miotics also may cause iris congestion and a plasmoid aqueous high i protein concentration. A peculiar irreversible

band keratopathy recently has been observed as a beal complication associated with the prolonged se of some proprietary pilocarpines.[19] This ffect may not be related to the pilocarpine but ather to the preservatives that are added to the ehicle or to other factors.

Pilocarpine can cause such systemic symptoms s profuse diaphoresis, salivation, nausea, vomiting, gastrointestinal cramping, bronchiolar spasm, ulmonary edema, and symptoms suggestive of cute abdomen.[20] Such occurrences are uncommon and generally have been seen only in the ged who have exceeded the usual frequency of lrug instillation.

In addition to pilocarpine, irreversible cholinesterase inhibitors such as diisofluorophosphate and chothiopate iodide in concentrations of 0.08 to 0.25% are frequently used topically in the management of glaucoma. The production of lens opacities is a recently recognized local complication to add to other local effects such as iritis, accommodative spasm, and cysts of the pupillary margin.[21-23] Echothiopate iodide also has been incriminated in the development of retinal detachment.

Cholinesterase inhibitors can be absorbed in concentrations sufficient to reduce the levels of red blood cell and serum cholinesterases. Because succinylcholine is hydrolyzed by serum cholinesterase, succinylcholine probably should be excluded from the anesthetic regimen of patients who are receiving topical therapy with cholinesterase inhibitors, because prolonged apnea might occur.[24-27] Anesthetic deaths have been noted in three cases in which topical diisofluorophosphate was used to treat glaucoma.[1] (Diisofluorophosphate is also used in children for the treatment of accommodative esotropia—an important fact when surgery is being considered.) The dangers of using these drugs in patients under treatment for myasthenia also must be recognized.

Other systemic effects of the topical cholinesterase inhibitors include gastrointestinal symptoms, primarily cramping but occasionally diarrhea and nausea, increased salivary, bronchial, or lacrimal secretions, and rarely cardiovascular or neurologic disturbances.[24] Symptoms of acute abdomen have occasionally resulted in laparotomy.[28] These symptoms are uncommon if the equivalent dose of echothiopate iodide is 0.06% or less.[29]

Topical Epinephrine.—Local effects of topical epinephrine drops include burning and sometimes production of a beefy redness of the conjunctiva, as well as the deposition of melanin-like oxidation products of epinephrine; these deposits most commonly accumulate as discrete material in the conjunctiva but may also rarely cause diffuse corneal changes suggestive of malignant melanoma.[30] Unfortunately, eyes have been enucleated for this benign condition. Topical epinephrine also can cause systemic symptoms of sympathetic stimulation, including anxiety, palpitation, and other symptoms.[31] These drops should not be used in patients using monoamine oxidase inhibitors such as tranylcypromine (Parnate) because paradoxic systemic hypertension may result.[1]

Systemic Agents

Acetazolamide (Diamox) and related synthetics are occasionally used as systemic supplements to the topical therapeutic agents in the management of glaucoma. The prolonged use of these agents can cause paresthesias, gastrointestinal disturbances, loss of potassium, and occasional renal stone formation. Less likely known, however, is that acetazolamide may induce a reversible acute myopia as an ocular side effect.[2]

Steroids

Topical Steroid Therapy

Many ocular complications have been documented as a direct result of steroid therapy. The topical application of steroids potentiates fungus corneal ulcers and herpes simplex keratitis, elevates intraocular tensions in certain susceptible individuals causing on occasion irreversible glaucoma, induces the formation of cataracts, and retards local wound healing. Mitsui and Hanabusa[32] have shown the dramatic effect of topical steroid therapy on conjunctival flora. In their experiments, the recovery of fungus isolates changed from 0 to 50% after two weeks of topical steroid treatment. This may be a significant reason why steroids are increasingly incriminated in the rising incidence of keratomycoses.[33] Corneal ulcers seem to be adversely affected by steroids. Herpes simplex keratitis seems to be reactivated with greater than normal frequency after topical steroid use and once infection has been established, steroids significantly reduce resistance of the cornea to the virus.[34-37]

Topical steroids administered four times a day during a six-week period have caused a significant increase in intraocular pressure in more than 30%

of the normal population[38-40] (greater than 90% in a population with open-angle glaucoma[39]). In some instances, this has produced glaucomatous field defects[41] and irreversible glaucoma, though usually these effects are transient and the eye returns to pretreatment conditions when therapy is stopped. Although most of the studies of the induced-pressure increases have used 0.1% dexamethasone, other topical steroid preparations also can induce glaucoma; a notable exception may be medrysone.[42,43]

Topical steroids have retarded corneal wound healing under controlled experimental conditions. A recent report suggests that this retardation may be clinically significant. Stigmata of poor wound healing after cataract extraction included unintentional filtering blebs acquired frequently in the group of postcataract extraction eyes treated with topical steroids, compared to none in the control eyes treated with placebo drops.[44] Additionally, topical steroids may cause mydriasis and ptosis.[45]

Considering these many complications it is important that topical medications containing steroids be used only with specific indications and for a limited time.

Although no systemic symptoms have been related to the topical use of steroid agents, some systemic absorption appears to take place.

Nursall[46] showed a decrease in the quantity of circulating eosinophils after several days of topical therapy. Burch and Migeon[47] also demonstrated a decrease in the amount of urinary 17-ketosteroids collected during a 24-hour period after the topical application of dexamethasone.

Systemic Steroid Therapy

With the possible exception of activating herpes simplex and fungus keratitis, systemic steroids may cause all of the ocular complications previously noted. A recent study suggests that approximately 20% of patients who were given more than 15 mg of prednisolone each day (or its equivalent) for between two and eight years will develop complicated cataracts. Systemic steroid-induced glaucoma, though observed, is rare.[48]

Other Anti-inflammatory Agents

Chloroquine and Related Drugs

The retinopathy induced by chloroquine is dose-related. A total dose of as little as 100 gm may produce a retinopathy[49] that usually becomes manifest initially in the posterior pole where a delicate derangement of the pigment epithelium may be seen in the paramacular or parafoveal regions. These changes become more apparent with time and eventually may produce the bull's-eye appearance that is characteristic of advanced disease or, when more severe, a clinical appearance indistinguishable from advanced retinitis pigmenta.[49] After discontinuance of the use of the drug, the retinopathy may continue to worsen although this is not inevitable. In a long-term follow-up study, Carr et al.[50] found that of patients who had retinopathy when drug therapy was stopped, 12% improved, 64% showed no change and 24% became worse.

Early symptoms of chloroquine toxicity include difficulty in adjusting to bright lights and occasionally photophobia. These symptoms probably are related to the retinal toxicity.[51] The most common visual symptom noted by Percival and Behrman[52] was a transient aggravation of presbyopic symptoms, which was seen soon after initiation of therapy. In the early stages, central visual acuity may be normal in spite of a dense pericentral ring scotoma. Eventually, central vision may be lost, and with further retinal damage, nearly the entire visual field may be lost. Although alteration of red light thresholds was considered one of the first functional changes in chloroquine retinopathy,[53] it was not observed in all of Krill and associates'[54] patients.

No test will consistently provide unequivocal information of early retinal toxicity. Careful fundus examination at intervals after an initial pretreatment base-line evaluation still is the most practical method for the evaluation of potential retinal toxicity. In some instances, serial fundus photographs will be helpful, especially if some derangement of the pigment epithelium was present at the pretreatment examination. That objective serial fundus evaluation is important is supported by the observations of Nylander,[53] who found that 70% of patients with retinopathy had no subjective complaints. Nylander suggested that combining fundus examinations with perimetry and electroretinography would more consistently detect patients who had retinopathy. At this institution, serial fundus examination is frequently accompanied by fundus photography and fluorescein angiography.

Corneal changes are not uncommon in patients receiving chloroquine. These changes are functionally benign and disappear within months after therapy is discontinued.[54-55] The retinopathy may

appear without the keratopathy.[56] At this institution, we do not consider keratopathy a reason to discontinue chloroquine therapy.

Indomethacin

One author believed that indomethacin produced keratopathy reminiscent of the changes seen with chloroquine and physiologic alternations in the retina expressed as diminished voltage in the electroretinogram.[57] My colleagues and I have not recognized these complications.

Sodium Salicylate

High doses of sodium salicylate over short intervals may cause a temporary blindness, either complete or partial.[2]

Cardiovascular Drugs

Digitalis

Probably the most well known ocular effects of cardiovascular drugs are those related to digitalis toxicity. The reported incidence of ocular manifestations of digitalis toxicity has been estimated to be as high as 25%. These ocular manifestations may occur before other toxic symptoms.[61]

The most common ocular symptoms of digitalis toxicity are blurred vision and disturbed color vision. Both a transient and a permanent amblyopia accompanied by central scotomas have been described. Yellow vision is common, but green, blue, and red vision also have been noted. Occasionally, objects appear grayish or white as if covered with snow. Yellow vision, although classically suggestive of digitalis toxicity, also has been noted after chlorothiazide, marihuana, amyl nitrite, the sulfonamides, quinacrine, and streptomycin.[2,58] Experimental studies showed elevated dark-adaptation thresholds in normal human subjects who were given therapeutic nontoxic doses of digitalis.[59]

Parenterally administered digoxin lowers intraocular pressure as a consequence of a decrease in aqueous formation.[60] This effect is not sufficient to make digitalis practical in the management of glaucoma.[61]

Nitroglycerin and Amyl Nitrite

Nitroglycerin and amyl nitrite may cause a very brief increase in intraocular pressure in association with vasodilation. This is apparently the basis for occasional warnings against the use of nitroglycerin in the presence of glaucoma. Grant,[2] however, was unable to find any case reports in which nitroglycerin or amyl nitrite precipitated an attack of glaucoma.

Spironolactone

Spironolactone (Aldactone) is an aldosterone inhibitor that reduces aqueous flow, thought it is not an effective agent for the treatment of glaucoma.[1]

Antibiotics

Topical chloramphenicol used over prolonged intervals occasionally has caused hypoplasia of the bone marrow.[62] Topical neomycin, a common ophthalmic preparation, causes local hypersensitivity. Accordingly, it should not be commonly used as a first choice agent in the treatment of minor ophthalmic infections.

Among the systemic antibiotic agents, the sulfonamides probably have accounted for the greatest frequency of toxic ocular effects.[2] Toxic amblyopia secondary to sulfonamide therapy has been reported.[63] Grant[2] discussed the precipitation of an acute and completely reversible myopia by the use of sulfa drugs. The myopic change, which may amount to several diopters, is believed to be related to a change in the refractive property of the lens itself. The tetracyclines also have precipitated acute myopic change.[64]

Ethambutol, a drug used to treat tuberculosis, has caused involvement of the neuro-optic pathways. Its toxicity has been the subject of several experiments in primates.[65] Two patients receiving sparsomycin, an antibiotic used as a cancer chemotherapeutic agent, experienced blurred vision in association with ring scotomas and pigment changes in the macular region.[66]

Optic neuritis frequently has been associated with chloromycetin[2,67,68] and less frequently with isoniazid and streptomycin.[2]

Phenothiazine Derivatives

In 1960, Apt[69] summarized the complications of ocular side effects seen with the phenothiazine tranquilizers. Oculogyric crises have been seen with most of these drugs. Chlorpromazine was recognized as a cause of photosensitivity, and thioridazine was considered a cause of pigmentary degeneration of the macula, which was associated with visual loss, a constricted field, and abnormal dark adaptation. (Although thioridazine has produced retinal changes in dosages considered to be therapeutically safe, such occurrences are rare; the changes usually have occurred after prolonged use of higher dosages.)[70] In 1964, ocular pigmentation was noted in association with skin pigmentation after prolonged chlorpromazine therapy.[71] Ocular findings include pigmentation of

the lids (sometimes purplish in color) and exposed regions of the conjunctiva; golden brown granules in the epithelium and deep stroma of the cornea near the endothelium; and axial lens changes characterized by white or brownish yellow granules concentrated in the anterior subcapsular areas. In DeLong and associates'[72] review, no patient who received less than 500 gm experienced lens changes; corneal changes occurred only if patients received more than 100 gm; among patients who received more than 2,500 gm, 90% had lens changes.

Vision is not commonly affected by lens change, though a patient described by Trediei et al.[73] had a chlorpromazine-induced cataract that reduced vision. Additional less common complications include pigmentary clumping in the retina, retinal vessel attenuation, and disk pallor.[74] Apparently some of the deep corneal changes may regress slowly when the medication is discontinued.[75]

Gynecologic Drugs

Oral Contraceptives

Oral contraceptives have been associated with various ocular abnormalities. In one study,[76] however, the ocular findings of 212 patients using different oral contraceptive products were compared with ocular findings and symptoms in 50 normal control patients. No ocular disease or change was found in the treatment group that could not be expected in the random sample of the population. Walsh et al.[77] are maintaining a file on the reports of ophthalmic disease that has been suspected to be related to "the pill." An intolerance to contact lenses has occasionally occurred in patients who were previously wearing the contact lenses comfortably.[78,79]

Clomiphene

Clomiphene, an ovulatory-stimulating drug used in the treatment of female infertility, has produced transient scotoma in four of 58 patients. The retina was believed to be the site of toxicity.[80]

Topical Anesthetics

Topical anesthetics are commonly used in such routine procedures as removing foreign bodies and taking cultures for bacteria. These agents can delay healing of corneal abrasions.[81] Local anesthetics also have potent antibacterial and antifungal properties.[82-86] A recent prospective clinical study showed that bacterial recovery from the conjunctiva was significantly inhibited after instillation of commercially available proparacaine (Ophthaine).[87]

Miscellaneous

Ophthalmologists and neurologists are generally aware that many drugs (for example, opiates, barbiturates, diphenylhydantoin, ethyl alcohol) may induce ocular nystagmus.[88]

L-dopa may induce exaggerated symptoms of oculogyric crises in patients subject to these crises prior to therapy.[89] Additionally, *L*-dopa may produce a transient mydriasis that can be replaced by a significant and more chronic miosis.[90]

Miosis has been noted after opiates, reserpine and chloral hydrate, even in usual doses.[2] In addition to miosis, chloral hydrate may cause swelling of the lids and edema of the conjunctiva.[2]

A common manifestation of toxicity related to quinine, tobacco, and alcohol is amblyopia. Quinine poisoning is seen less now because the use of the drug has decreased. Nevertheless, toxic effects may occur in persons who are taking average doses, although it is more likely seen after an overdose. The effects range from a slight blur to complete blindness, which usually are partially reversible. Early ophthalmoscopic changes vary, but definite pallor of the optic nerve is seen later. The visual field defect in quinine amblyopia appears as a peripheral contraction.[91] Quinine also has been reported as a cause of iris atrophy.[92] Optic nerve hypoplasia after quinine ingestion has been noted.[93] Amblyopias of toxic origin are also associated with the long-continued use of tobacco or alcohol. Both eyes are usually affected with a characteristic centrocecal scotoma. Tobacco smoke from a pipe or in the form of cigars is generally necessary to produce this type of amblyopia,[94] but cigarette smoking has also caused this change. An interesting observation is reported by Parkinson,[95] who noted tobacco amblyopia primarily in older men who smoke cheap strong tobacco known as shag tobacco. After discontinuance of pipe smoking, visual improvement occurs. Some evidence shows that the effect of tobacco is ultimately related to a failure of detoxification of cyanide derived from tobacco smoke. Treatment with hydroxycobalamine may be effective in restoring vision.[96] This entire subject has recently been reviewed.[97] Alcohol amblyopia is probably a result of actual vitamin deficiency rather than a direct toxic effect of the drug.[94]

Vitamins A and D given in high doses have

produced adverse changes in the eye. Excessive vitamin D may produce calcific deposition in the cornea as a manifestation of hypercalcemia. This band keratopathy gradually disappears after cessation of the vitamin D.[2] Vitamin A in excess may produce loss of hair, which can include the eyelashes and eyebrows. A more significant problem perhaps is the development of increased intraocular pressure which causes papilledema. Four patients who had vitamin A intoxication with reversible papilledema were recently described.[98] Each patient was taking approximately 200,000 units of vitamin A each day for long periods, primarily for the treatment of acne. After cessation of the drug, the papilledema resolved very slowly.[98]

Cataracts have been associated with the use of several systemic drugs, some of which are no longer in use, such as triparanol.[99] Others, such as steroids, form a significant part of the therapeutic armamentarium of many practitioners. It has been suggested that dibromomannitol, an antimitotic agent that has been used in the treatment of chronic myelogenous leukemia, may cause posterior lens opacities.[100] Busulfan (Myleran) has been similarly incriminated.[2] Cataract production by these compounds is uncommon.

Prolonged use of eye drops of phenylmercuric nitrate was associated with a cataract that contained high concentrations of mercury.[101]

Signs of ocular toxicity were seen in 20 of 40 patients treated with vincristine sulfate for leukemia and other malignancies. These consisted of ocular muscle paresis and involvement of the fifth and the seventh nerve.[102]

The ocular abnormalities caused by thalidomide have been the subject of several reviews. Anophthalmia and colobomas were among the more severe defects. Paresis of the third and the sixth cranial nerve was not uncommon. Several children also had nasolacrimal duct obstructions.[103-105]

Visual disturbances have been related to the use of pheniprazine hydrochloride, a mono-amine oxidase inhibitor. This drug has been incriminated as a cause of optic neuritis.[106-108]

Transient visual hallucinations were noted in three patients treated with iminodibenzyl compounds (amitriptyline and imipramine) for depression.[109]

Reactions may follow intravenous fluorescein used as a diagnostic research tool in ophthalmology and occur in 0.6% of patients who undergo angiography. Although more than two thirds of the reactions were an allergic type characterized only by urticaria, more than one fourth were severe, often associated with a shock-like reaction.[110]

Summary

The ocular complications associated with topical and systemic medications are reviewed. Serious systemic manifestations may result from absorption of topically applied ophthalmic agents. The review considers anticholinergic agents, drugs used in the management of glaucoma, steroids and other anti-inflammatory medications, cardiovascular and gynecologic drugs, antibiotics, the phenothiazine derivatives, and others.

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(Continued to page 963)

"The history of science, and in particular the history of medicine ... is ... the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

– George Sarton, from "The History of Medicine Versus the History of Art"

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion

Results of a questionnaire to 7,000 physicians:

62.9%
Believe combination drug products are useful.

13.8%
Do not believe combination drug products are useful.

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion & Dialogue

Doctor of Medicine

Louis Lasagna, M.D.
Professor and Chairman
Department of
Pharmacology & Toxicology
University of Rochester
School of Medicine
and Dentistry



Obviously, many drugs are given concomitantly. Whether it makes sense to combine medications in one preparation, be it capsule, tablet, or liquid, is a question that can be answered only by examining the advantages and disadvantages in the individual case.

Among the advantages is, first of all, convenience. The more medications that are taken concurrently and the more complicated the directions, the less likely the patient is to take medications accurately. From the standpoint of convenience and accuracy, and economy as well, you can make an important case for putting medications together in one preparation, as long as they are compatible.

By the same token, when you prescribe a properly tested and rational combination, you should have less worry about pharmaceutical or pharmacological compatibility – and about reasonable dosage ratios as well. Compatibility of the formulation should be demonstrated in the laboratory and clinic before the product is available for prescription—which is more than can usually be said for the physician's own spontaneous creations. And, the dosage ratios employed in rational precompounded combinations are designed to meet the needs of substantial numbers of "typical" patients.

There is no doubt that many "atypical" patients are to be found, and for them the prefabricated combination must be rejected. But that hardly argues for eliminating rational combinations from the market. Think, for example, of the problems that would arise if the components of widely accepted combinations, like the oral contraceptives and the diuretic-antihypertensives, always had to be prescribed, purchased and ingested separately.

One disadvantage that comes to mind is some doctors' unawareness of the ingredients a given combination contains. For example, a doctor might know that a patient is allergic to aspirin but forget that a certain analgesic mixture, which he knows only by its trade name, contains aspirin. His prescription, then, causes considerable discomfort, to say the least. This problem is a function of physician education, rather than of combination therapy as such. Improving doctors' knowledge about all medicaments they prescribe is a problem that deserves tackling on its own.

Another accusation leveled at combination drugs is that they encourage sloppiness of diagnosis and treatment. In many cases, however, a combination may prove to be the most effective choice. A good example of the usefulness of combinations appears in a recent article in the *Journal of Chronic Diseases* on the efficacy and side effects of an antihypertensive containing three ingredients, in which the track records of the combination drug and the individual ingredients were compared. Interestingly enough, whether the drugs were given individually or together, incidence and severity of side effects were the same. But blood pressure control was invariably better when the drugs were taken in one combination tablet than when they were taken separately (in "titratable" dosage) or in two or three different tablets.

Deciding which combinations constitute rational therapy obviously leads to a discussion of who is to determine which should be used and which should not. Realistically, I think combinations should be evaluated somewhat differently if they are old and established or new and untried.

In today's regulatory atmosphere, there is no possibility of a new combination being put on the market without a substantial amount of acceptable evidence in the form of controlled trials that show it to be safe and efficacious. On the other hand, I believe a different set of standards should apply to combination preparations that have been around for a long time. In other words, physician acceptance over a long period should be given some weight as evidence of the efficacy and safety of these drugs.

The FDA, however, does not seem to share this attitude. It often requires, for these older products, controlled trials that will monopolize the time of already overtired investigators and cost a great deal of money. I wish we could agree on a "grandfather clause" approach to combinations that have been around for a number of years that have an apparently satisfactory track record.

For example, I think some of the antibiotic combinations that were taken off the market by the FDA performed quite well. I am thinking particularly of penicillin - streptomycin combinations that physicians—especially surgeons—were given by injection. This made for less discomfort for the patient, less demand on nurses' time, and fewer opportunities for medication errors. To take the combination preparation off the market doesn't seem to be good medicine, unless actual experience showed a great deal of harm from the injudicious (rather than the proper use) of the combination.

The point that should be emphasized is that both fixed combinations are both rational and irrational combinations. The real question is, who is to determine which is which? Obviously, the FDA must play a major role in determining this determination. In fact, I don't think we can avoid taking the ultimate responsibility, but it should enlist the help of consultant physicians and experts in assessing the evidence and in making the ultimate decision.

Maker of Medicine

V. Clarke Wescoe, M.D.
President
Vnthrop Laboratories



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combinations generally. Ohviously, no one should be exposed willy-nilly to the potential side effects of two or three antihiotics wben only one is needed. At the same time there are cases where it is prudent to prescrihe more than one. Tbe clinician is the judge in these circumstances, as he should be.

There is no clear definition of the word rational. Most persons, I suppose, would find it synonymous with reasonable, but in many circumstances it may best he defined as the opinion of those in power at the moment.

Other factors govern combination therapy, not the least of which has heen its broad use hy practicing physicians anxious to achieve convenience in prescribing, to reduce medication error, and to save money for their patients. Combinations clearly have met the test on all three counts.

I have heen impressed by studies showing that the rate of error climhs markedly with the number of medications to he taken, even with sophisticated patients. When medically justified, therefore, this factor alone supports the logic of comhination therapy.

The cost argument for combinations appears to he irrefutable. In 1971, R. A. Gosselin studied the 71 combination products (excluding oral contraceptives) among the 200 most prescribed drugs. The study found that if all 71 products were discontinued, and if each ingredient in these combinations were prescribed separately, the price of medicines to patients would jump by $443.2 million on a national hasis! At a time when the cost of medical care is under so much fire, it would be nonsensical to boost costs without clearly irrefutable medical reasons.

The part played by government on this question, of course, is fundamental. The FDA should play a role in determining which combinations are reasonable. That role, as defined by law and regulation, is to ensure that any medication on the market is safe and effective in line with its label claims. Certainly combinations are entitled to as much consideration as single entities—neither more nor less. So long as the addition of one drug to another does not make either less safe, or less effective, so long as they are compatihle in a formulation, we have a reasonable product. It makes no sense to recommend the use of two products for certain conditions and to deny their being comhined in a single form. An unhappy side effect of the problem concerns the efficacy panel discussions of many products suhmitted for review. The term "effective, but" has heen freely interpreted to mean "ineffective" in toto, regardless of the merit of the individual drugs. This interpretation has placed numerous useful comhination products in needless jeopardy.

In reading the actual reports of the review panels, it seems clear that some of the ratings were based less on scientific research and clinical observation than on the "informed" opinions of the panelists. These "informed" opinions were accepted at face value, while the "informed" opinions of others who had used the products were rejected. All of this put combination products into a sort of scientific never-never land.

It should be kept in mind by all, government as well as others involved in our health care system, that advances in therapy are seldom made in leaps and bounds hut rather by small painstaking steps—and that some of these steps have resulted from research in comhination drugs as well as with single entities. Given the near-infinite biologic variation in patient response, this is hardly surprising to clinicians. It should not be to regulatory agencies either.

In the end, the practicing physician is in the best position to decide if a particular comhination makes sense. Such a decision should not be made exclusively hy those whose responsibility for continuing clinical care is limited. Clinicians are the best judges of efficacy because the ultimate proof of any product's effectiveness is acceptance hy physicians who have observed its actions in patients over time. The corollary statement may be made about over-the-counter medicines, which would not long survive if they failed to afford the relief the user anticipates. That the antihistamine in a "cold" remedy may not *always* be necessary is no reason to proscribe the comhination generally.

Opinion & Dialogue

What is your opinion, doctor?
We would welcome your comments.

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Fracture Conference

Intercondylar T-Fractures

RICHARD S. BRYAN, M.D., JOHN A. WELSCH, M.D. AND
EINER W. JOHNSON, JR., M.D.

r. Richard S. Byran:

The intercondylar fracture, the so-called fracture or Y-fracture of the elbow, is a serious acture; but fortunately it is not common.

r. John A. Welsch:

The recent literature on intercondylar T-fractures of the humerus in adults reveals wide disagreement among orthopedists, first, in treatment nd second, in methods of evaluating end results.

Most of the vascular and neurogenic structures ourse through the anterior compartment of the bow, but the ulnar nerve courses around the edial epicondyle to the posterior compartment. ailure to restore the balance of muscle power, as ell as the articular surface, will lead to a poor nctional result. Normal range of motion of the lbow is flexion from 0 to 150° and pronation nd supination from 0 to 90°.

In a 12-year period, only 52 isolated T-condylar actures of the lower end of the humerus were een at the Massachusetts General Hospital. Few ases can be found in the recent literature. Riseorough and Radin[1] reported 29, Bickel and erry[2] included 17, and Miller[3] noted only 11 uch fractures.

The mechanism of this injury is a direct blow n the olecranon, which is then driven as a wedge pward between the humeral condyles. Typically, he fracture is due to a fall on the flexed elbow. n the cases reviewed, one such fracture occurred n a patient whose elbow was jutting from a car window and was struck by an object.

The treatment of the T-fracture can be divided nto three main types: (1) open method, which includes open reduction and anatomic assemblage of he fragments, with internal fixation and external support, (2) closed method, which includes manipulative reduction and plaster immobilization in a position of stability, or skeletal traction through an olecranon pin, or the collar-and-cuff or "bag of bones" treatment, and (3) combined method, which is an open reduction with internal fixation of the articular fragments, followed by closed manipulation of the supracondylar element of the fracture. Each treatment has advantages and disadvantages.

Closed manipulation followed by plaster immobilization frequently fails because most fractures of the elbow joint have very little natural stability and the maintenance of the reduction is uncertain. When stability is obtained in full extension, motion is not readily recovered at the elbow joint. Traction with or without manipulation is frequently unsuccessful because of the rotational pull on the condyles through the collateral ligaments and muscles. Early arthroplasty in a badly shattered elbow often gives a weak and unstable joint. Surgical intervention also carries the risk of infection and the possibility of periarticular adhesions.

Generally, the complications associated with T-fractures are loss of motion due to periarticular fibrosis, capsular contraction, bone block, or residual deformity; ulnar nerve palsy; instability; avascular necrosis of one of the fractured fragments; myositis ossificans; and skin necrosis.

In the surgical treatment of this type of fracture, the main objective is to achieve fixation so that early motion can be started. Two surgical approaches can be used. Bickel and Perry[2] and Miller[3] preferred the posterior approach as recommended by Speed[4] and Van Gorder.[5] Cassebaum[6] described a transolecranon approach. The main limitation of these approaches is the inability to visualize the vascular and neurogenic structures in the anterior compartment. In these approaches, the patient is placed prone, with his forearm hanging over an arm board. In the Van Gorder[5] approach a tongue of triceps is reflected, and the fractured fragments are visualized (Figure 1). The same approach can be used in the over-the-chest position. Various methods of internal fixation can be used: Kirschner wires (both plain and

Fracture Conference March 31, 1969.

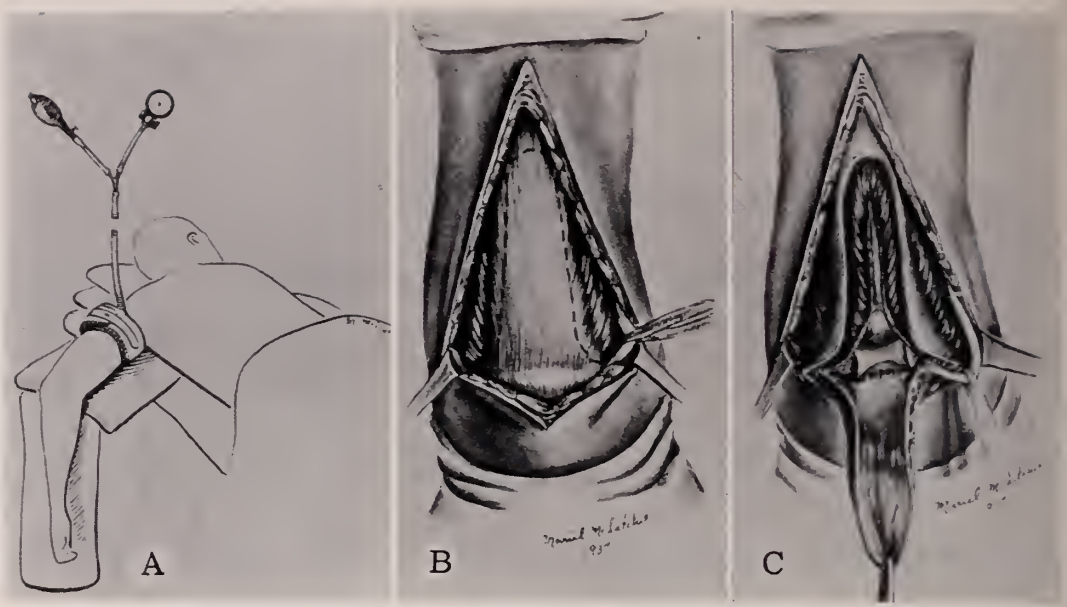


Fig. 1—Posterior approach to elbow in intercondylar T-fractures. *(A)* Position of patient on operating table, with tourniquet in place and line of incision. *(B)* Triceps muscle and ulnar nerve exposed. Dotted line shows how triceps fascia is cut. *(C)* Incision has been deepened through triceps muscle and continued outward and inward to tips of both condyles, dividing completely the muscle expansions but avoiding the ulnar nerve. (From Van Gorder, G. W.: Surgical Approach in Supracondylar "T" Fractures of the Humerus Requiring Open Reduction. J Bone Joint Surg n.s.22:278, 1940. By permission.)

threaded), screws, or "Y-plates." Basically, an attempt is made to restore the joint line first and then to fix the distal fragments to the humeral shaft.

Regardless of treatment, some restriction in motion can be expected in flexion and extension. Rarely is loss of pronation or supination a problem with this type of fracture.

Case Reports

Case 1

A 19-year-old girl fell from a motorboat and was struck by the propeller blade. Examination revealed a depressed open skull fracture and a laceration of the right elbow, with bone protruding. The initial roentgenogram showed a comminuted fracture of the condylar area of the right humerus (Figure 2). The initial treatment consisted of immediate craniotomy, with evacuation of a subdural hematoma, and debridement of the elbow fracture. The elbow fracture was then packed open, and the patient was placed in "side-arm" traction; three weeks later she was placed in a plaster cast. Six months after injury, she had flexion of 77 to 157° and full pronation and supination.

Case 2

A 19-year-old boy tripped and fell directly on his left elbow. The roentgenogram showed a displaced comminuted fracture of the left elbow in the supracondylar area (Figure 3 *A*). At surgery, the medial condyle was fixed internally to the lateral condyle and the remainder of the fracture was placed in traction. The ulnar nerve was translocated, and skeletal traction was applied. The



Fig. 2 (Case 1)—Intercondylar T-fracture. Initial roentgenograms. *(A)* Anteroposterior view. *(B)* Lateral view.



Fig. 3 (Case 2)—Intercondylar T-fracture. *(A)* Initial Anteroposterior view. *(B)* After surgery.

postsurgical roentgenograms show the medial fragment with a screw and the arm in skeletal traction (Figure 3 *B*). Roentgenograms were obtained six months after surgery when the patient had a range of motion almost identical to that of the first patient.

Case 3

A 62-year-old woman fell down the steps at her home and landed on her flexed elbow. She was placed in a posterior plaster cast at another institution and was referred here three days after injury.

Initial roentgenograms were taken (Figure 4 *A*). Examination at our clinic revealed a moderately swollen left elbow with a clean, sutured, 2-cm laceration on the posterior aspect of the left elbow. Nerve function and circulation were intact. Seven days after her injury, she underwent open reduction and internal fixation of the left distal humerus, with insertion of a Y-Vitallium plate and nine screws. The ulnar nerve was freed from the groove at surgery and was intact.

Motion was begun after 21 days. Four weeks after surgery, the patient had ulnar neuropathy; and 10 weeks after surgery, mild but definite ulnar nerve weakness was noted, with slight atrophy of the intrinsic muscles of the hand. When last seen eight months after surgery, she had a range of motion of 35 to 140° and had regained full pronation and supination. She had no sensory loss. Final films were taken eight months after surgery (Figure 4 *B* and *C*).

Case 4

A 64-year-old woman fell down some steps and landed on her right elbow, incurring a severely comminuted fracture of the supracondylar region. Sensation and circulation were intact. Three days after fracture, she underwent open reduction and internal fixation of the distal humerus with nine K-wires (Figure 5 *A*). Three and one-half weeks after her initial injury, the cast was removed and gentle active motion was begun. Six and one-half weeks after surgery, the K-wires were removed. When last seen, 14 weeks after her initial fracture, she had a range of motion of 45 to 90°, with full supination



Fig. 5 (Case 4)—Intercondylar T-fracture. *(A)* Anteroposterior view at surgery. *(B)* Final lateral view. Note bone block anteriorly.



Fig. 4 (Case 3)—Intercondylar T-fracture. *(A)* Anteroposterior view on admission. *(B)* Final lateral view. *(C)* Final anteroposterior view.

and pronation at the elbow (Figure 5 *B*).

Comments

Dr. Bryan:

Kirschner wires tend to slip when utilized in fixing this type of fracture, unless many are used. Even nine Kirschner wires did not prevent some slippage of the fracture in Case 4. The grossly comminuted fracture cannot be held with any fixation. There is no way you can put a "bag of bones" together. However, there is no great harm done in attempting fixation by use of wires if the fragments are not dissected too extensively. Knight[7] advocated excision of the proximal portion of the olecranon to increase the range of motion in flexion and extension. Cassebaum[6] described an approach in which he simply osteotomized the olecranon and reflexed the triceps in order to get exposure. This concept is based on the observation that the olecranon fossa becomes filled with bony callus, producing a block to full motion. Therefore, if a portion of the olecranon is excised, the chances of regaining flexion-extension motion in this fracture are enhanced.

The first patient (Case 1) had an obviously dirty wound, and there was no choice except to use traction. This fracture would have been classified as a type II according to Riseborough and Radin,[1] because the fragments were not rotated. These patients do well any way you treat them. The one-screw technique is an excellent method of treating this type of fracture.

The second patient (Case 2) had a radial palsy prior to surgery. After surgery he also an ulnar palsy. Both nerves recovered completely.

The third patient (Case 3), an elderly woman, also had ulnar neuropathy despite the visualization and careful protection of the ulnar nerve.

Dr. Anthony J. Bianco, Jr.:

I wonder why many experts like Kern-Cohen[8] from Australia take the opposite view and say that these fractures need not be opened. Nonunion is very rare in this region, and this is not a weight-bearing joint. But you do want to regain motion. If you get good, painless motion, this is what you are after. What do you think?

Dr. Bryan:

This is exactly the viewpoint of Riseborough and Radin.[1] We could go back to an earlier time and quote Philip Wilson[9] reporting from the same hospital who believed in the open reduction of at least some of the fractures. He did not believe that the grossly comminuted fractures in th elderly required open reduction.

Dr. Bianco:

I agree. I think the young adult who sustai injury to this region should be operated on, bu I wonder if operative intervention does not pr mote reduced motion in the elderly.

Dr. Bryan:

There is no question that operation decreas motion in the elderly when the fracture is grossl comminuted. In the younger patient, howeve operative intervention should give a better en result. Bickel and Perry[2] got better results in th operative cases of comminuted fractures the reported.

One comment can be made regarding patie position during operation. To operate on an obes patient in the prone position is a mistake, becaus the fracture cannot be exposed adequately. Oper ation is best done with the arm over the che and the patient supine.

Dr. Bianco:

In the operative case, do you think the ulna nerve should be translocated every time?

Dr. Bryan:

I think that it should be exposed every time but translocation of the nerve can cause trouble and perhaps the nerve should be left in its groove

Dr. Charles F. Mess:

For the third patient (Case 3) who had ulna nerve neuropathy, why was not something don about the neuropathy at operation? The neurop athy had become worse within a week or two and went from a tingling to paresthesia.

Dr. Bryan:

Nothing was done about the neuropathy be cause it was not noted at operation. The woman was at home during the time that the neuropathy developed. She was improving when she returned

Dr. Charles P. Fina:

Mention was made of primary treatment o excision of fragments and arthroplasty. Are there any comments from the literature on the result of these?

Dr. Bryan:

This was done in the earlier years, and the results were good, but the treatment left a weak elbow. The key to success was never to excise bone above the condyles. If the capitellum alone was excised, an excellent result was obtained. The capitellum and the trochlea can be excised, but the condyles cannot. If they are, too much weak

ess and instability result.

Dr. James H. Dobyns:

Perhaps another point deserves elaboration. Obviously, early motion is essential and useful, but the questions are how early and on what do you base this decision.

Dr. Bryan:

If internal fixation is used, motion should be begun at three weeks. If the collar-and-cuff method is used, motion also should begin in about three weeks.

Dr. Welsch:

I believe that Miller[3] advocated motion at seven to 10 days in fractures that are securely fixed.

Dr. Bryan:

We are trying to combat what is called traumatic arthrofibrosis and similar soft-tissue adhesions around and in the joint structures. I realize every patient is a little different in this respect, but there must be some point in time where you could begin—when the pain and swelling have subsided.

I would think though that it is wiser to wait until the inflammation has subsided. In their report, on fractures of the radial head, Riseborough and Radin[1] advocated three weeks before motion is started, and their experience revealed that this gave better end results.

Dr. James S. Breivis:

I am interested in the absence of vascular injury. Is lack of such injury true for the four patients reviewed here or for all such patients reported on in the literature?

Dr. Welsch:

That includes the ones that were mentioned in the literature. There were no Volkmann contractures in the reports that I read.

Dr. Bianco:

Do you still use the Y-plate?

Dr. Bryan:

Yes. However, fixation by screws alone is better, if such fixation is possible.

Conclusions

1. Comminuted intercondylar T-fracture of the distal humerus is a serious injury that almost always produces some loss of elbow motion in flexion and extension.
2. In all but the elderly patient, open reduction and internal fixation is the method of choice.
3. Motion should be started early—no later than three weeks after injury—and continued until the recoverable range of function is maximal.
4. Occasionally, late surgical attack on the elbow joint for removal of bony overgrowth may increase motion.

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Proctology

The Division of Colon and Rectal Surgery of the Department of Surgery of the University of Minnesota Medical School in cooperation with the Minnesota Academy of Family Physicians will present a program in "Proctology" at the Nolte Center for Continuing Education on October 23-27, 1972. This program is conducted through the Office of Postgraduate Medical Education of the University of Minnesota Medical School. Fee: $160.00.

Laboratory Letter

The Probability of Abnormal 12-Channel Results in Normal People

When a physician orders multiple test profiles, he will observe a number of clinically well patients with one or two inexplicable abnormal results.

This is inevitable. Why? Because "normal range" is usually calculated as the Mean ± 2 Standard Deviations. Statistically this means that 95 percent of normal people will fall inside normal limits. It also means that five percent of normal people will fall outside the normal range.

One Test Vs Twelve Tests

This 95 percent approach causes little trouble if you're measuring one test. Being reasonable people, physicians expect a normal person to have a borderline abnormal test occasionally.

The trouble comes when you start measuring twelve tests at once. Then physicians complain about the large number of unexpected borderline abnormal results. Yet probability theory dictates that almost half of the normal people on whom you measure twelve tests will have at least one borderline abnormal test.[1,2]

100 Normal People

Let's take an example. Suppose you're screening 100 normal patients in your office.

You can express the probability that one of these patients has a normal value for a single test (say calcium) as 0.95. This means that 95 of the 100 patients will have a normal serum calcium.

But now take a second test, for instance, glucose. Assume the glucose result is independent of the calcium result. Again you would expect 0.95 (or 95 of the 100) patients to have normal glucose.

The Rub

Now the rub. What is the probability that one of these patients will have both a normal calcium and a normal glucose? Answer: 0.95 × 0.95 × 100, or 90 patients of the original 100. If you keep applying this law of probability to all twelve tests, you find that only 54 of 100 normal people will have all their tests within normal limits.

Here are other probabilities:

Probability of all tests normal	54%
Probability of one abnormal test	34%
Probability of two abnormal tests	10%
Probability of three or more abnormal tests	2%

What does this mean to you? It means that if you screen normal individuals with 12-channel chemistry graphs, borderline abnormal results are inevitable if the mean ± 2 Standard Deviations, or 95 percent confidence limits are used to define normal. It also means that many of these borderline abnormal results will be clinically insignificant.

Richard L. Reece, M.D.
Minneapolis, Minnesota

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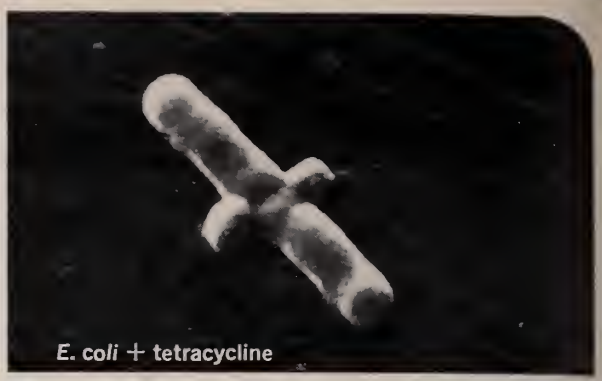
Encounter under the Scanning Electron Microscope



SEM reveals changes in *E. coli* exposed to antibacterial agents

The Scanning Electron Microscope (SEM) is the only instrument which gives 3-dimensional views on a microscopic level. This permits the surface morphology of microorganisms to be observed in detailed perspective. Changes in surface morphology of *E. coli* exposed to various antimicrobial agents are seen on the following page. An SEM photomicrograph of normal control *E. coli* appears above.









Different modes of antibacterial action — Similar changes in morphology

As part of a series of experiments,[1-3] strains of *E. coli* proven susceptible to each antibacterial agent were exposed to 1 MIC of the respective antibacterials for a three-hour period. Included were cell-wall-active drugs, ampicillin and cephalothin; a drug interfering with intracellular protein synthesis, tetracycline; and a chemical agent which acts by interference with para-aminobenzoic acid, sulfamethoxazole.

As seen above, elongation of the bacilli, mid-cell defects and spheroplast-like forms may be appreciated with the SEM technique. These changes in bacterial morphology were similar ... regardless of the antibacterial agent used and irrespective of its mechanism of action.

"At present, the significance of these observations in clinical infection must be considered with caution, but it is hoped that these data will stimulate a reevaluation of present concepts of the nature and role of morphological variants of bacteria exposed to a variety of antibacterial factors."[2]

It should be noted that no clinical conclusions can be drawn from this study, as it is not always possible to extrapolate *in vitro* data to humans.

References: 1. Klainer, A. S.; Fass, R. J., and Perkins, R. L.: Scientific Exhibit presented at the 25th American Medical Association Clinical Convention, New Orleans, La., Nov. 28-Dec. 1, 1971. **2.** Klainer, A. S., and Perkins, R. L.: *Antimicrob. Agents Chemother., 1*:164, 1972. **3.** Klainer, A. S.: Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A be hemolytic streptococcal infections and will not eradicate prevent sequelae (rheumatic fever, glomerulonephritis) of su infections. Deaths from hypersensitivity reactions, agranulocy sis, aplastic anemia and other blood dyscrasias have been ported and early clinical signs (sore throat, fever, pallor, purpu or jaundice) may indicate serious blood disorders. Frequent C and urinalysis with microscopic examination are recommend during sulfonamide therapy. Insufficient data on children unc six with chronic renal disease.

Precautions: Use cautiously in patients with impaired re or hepatic function, severe allergy, bronchial asthma; in gluco 6-phosphate dehydrogenase-deficient individuals in whom do related hemolysis may occur. Maintain adequate fluid intake prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytos

Encounter in Clinical Practice

Control of primary bacterial offenders

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B.I.D./T.I.D. dosage for around-the-clock coverage

Subsequent 1-Gm doses provide up to 12 hours of antibacterial coverage. More severe u.t.i. may require a q. 8 h. dosage regimen. Either schedule provides coverage during the waking and sleeping hours—especially important during hours of sleep when normal urinary retention tends to favor bacterial proliferation.

Also effective in nonobstructed chronic and recurrent u.t.i.

It is not uncommon for the elderly and the debilitated to develop chronic and/or recurrent nonobstructed urinary tract infections such as pyelonephritis and cystitis. Such cases often respond satisfactorily to Gantanol. The increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents including sulfonamides, especially in chronic or recurrent u.t.i.

Your Option: Tablets or Suspension

Either dosage form—the Tablets or the pleasant-tasting, cherry-flavored Suspension—can provide the dependable antibacterial activity necessary to control susceptible nonobstructed cystitis and pyelonephritis. Symptomatic improvement may usually be expected in 24 to 48 hours. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake. Gantanol (sulfamethoxazole) is generally well tolerated with relative freedom from complications; the most common side effects are nausea, vomiting and diarrhea. Frequent c.b.c.'s and urinalyses with microscopic examination are recommended.

In nonobstructed cystitis and pyelonephritis due to susceptible organisms

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necrolysis, urticaria, serum sickness, pruritus, exfoliative
matitis, anaphylactoid reactions, periorbital edema, conjunc-
l and scleral injection, photosensitization, arthralgia and
rgic myocarditis); *gastrointestinal reactions* (nausea, emesis,
ominal pains, hepatitis, diarrhea, anorexia, pancreatitis and
natitis); *CNS reactions* (headache, peripheral neuritis, men-
depression, convulsions, ataxia, hallucinations, tinnitus, ver-
and insomnia); *miscellaneous reactions* (drug fever, chills,
c nephrosis with oliguria and anuria, periarteritis nodosa and
phenomenon). Due to certain chemical similarities with
ne goitrogens, diuretics (acetazolamide, thiazides) and oral
oglycemic agents, sulfonamides have caused rare instances
goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

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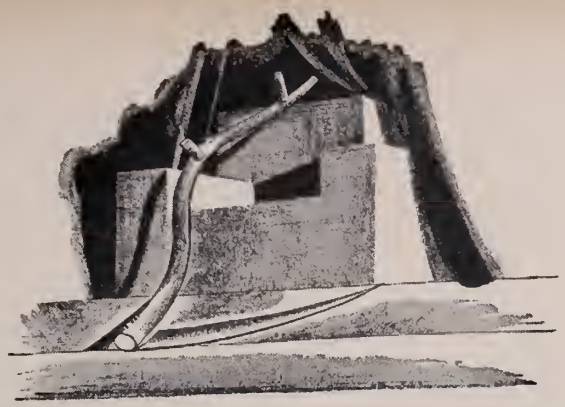
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In Memoriam

'Tis true; 'tis certain; man though dead retains part of himself; the immortal mind remains—Homer

CARL J. MARTINSON, M.D.

Dr. Carl J. Martinson, 84, Wayzata surgeon, died July 25. Born in Stillwater, Minnesota, Dr. Martinson obtained his medical education at the College of Medical Evangelists in Loma Linda, California. He interned at the Los Angeles General Hospital and practiced in California until in 1927 when he moved to Wayzata.

Dr. Martinson is a member of the Hennepin County Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Alma, and two sons, Doctors Arthur J. of California and Elmer J. of Wayzata.

CECIL A. WILMOT, M.D.

Dr. Cecil A. Wilmot, 61, Litchfield physician, died July 19. He was born in St. Charles, Minnesota, and obtained his medical education at the University of Minnesota.

Dr. Wilmot was a member of the Mid Minnesota Medical Society, the American Medical Assocation and the Minnesota State Medical Association.

He is survived by his wife, Isabel, and a son, Dr. Thomas of Winona.

SHU KANG HO, M.D.

Dr. Shu Kang Ho, 50, staff anesthesiologist at Bethesda Hospital, died July 17. He was born in Chekiang, China, and obtained his medical education at the National Medical College in China. He did postgraduate work at the University of Minnesota for three years.

Dr. Ho was a member of the Ramsey Medical Society, the American Society for Anesthesiologists, a Diplomate of the American Board of Anesthesiologists, a member of the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Beverly, four sons and two daughters.

FRANK R. GRATZEK, M.D.

Dr. Frank R. Gratzek, 73, retired Minneapolis radiologist, died July 18. He had been affiliated with the former St. Andrew's Hospital and St. Mary's and the University of Minnesota Hospitals. Dr. Gratzek also served as an instructor in radiology at the University of Minnesota Hospitals.

A graduate of the University of Minnesota Medical School, Dr. Gratzek was a member of the Hennepin County Medical Society and the American Medical Association and an associate member of the Minnesota State Medical Association.

Dr. Gratzek is survived by his wife, Mary.

JAMES H. BENDER, M.D.

Dr. James H. Bender, 64, Brainerd physician, died July 4. He was born in Two Harbors and had resided in Brainerd for the past 26 years.

He was founder and a member of the Lake Region Clinic, a member of St. Joseph's hospital medical staff, the Upper Mississippi Medical Society, the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, Alice, two sons, Ronald and Robert, and two daughters, Kathryn and Mary.

HENDRIK J. SVIEN, M.D.

Dr. Hendrik J. Svien, Rochester neurosurgeon associate professor of neurologic surgery in the Mayo Foundation Graduate School, died June 29. He was born at Dennison, Minnesota, and obtained his medical education at the University of Minnesota Medical School.

Dr. Svien was a member of the Mayo Clinic, the Society of Neurological Surgeons, the Zumbro Valley Medical Society, the Minnesota State Medical Association and the American Medical Association.

He is survived by his wife, Nancy, and two children.

LILLIAN L. NYE, M.D.

Dr. Lillian Nye, 87, St. Paul chemist, physician and humanitarian, died July 28. She was in Yale University Medical School's first class that graduated women and later shifted to the University of Minnesota where in later years she was honored as one of its distinguished "emertius" graduates. She had her B.S. and M.A. degrees in chemistry and taught the subject at the University of Minnesota before entering medical school. In addition, she was the first women physician in the St. Paul public schools, and it was her influence that developed family nursing service clinics first at Ancker Hospital.

Her diplomas and testimonials were many—life membership in the American College of Physicians and the American Academy of Pediatrics, Distinguished Alumnus of the University of Minnesota, recipient of the Girl Scouts' Golden Eaglet award, recipient of the University of Minnesota Outstanding Achievement Award and membership in many Canadian and foreign honorary medical societies. In addition she was a member of the Ramsey County Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

She is survived by many nieces and nephews.



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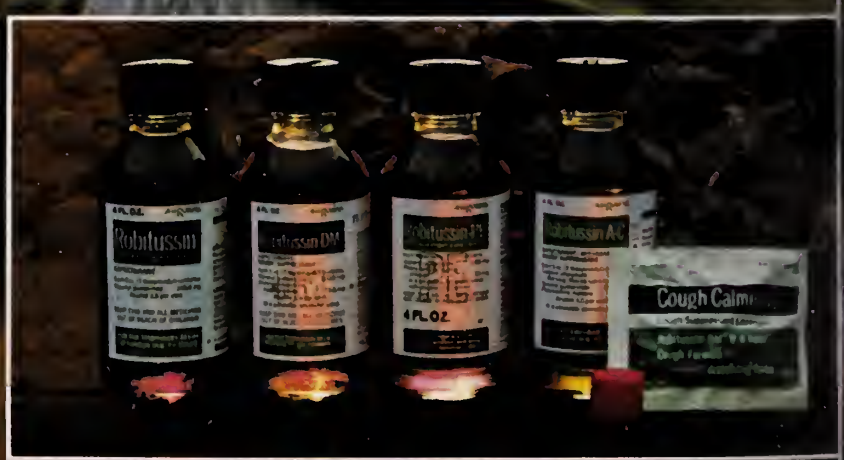
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performed. Lincocin has proved
aluable in treating patients hyper-
sitive to penicillin or cephalosporins,
ce Lincocin does not share
genicity with these compounds.
However, hypersensitivity reactions
ve been reported, some of these in
gents known to be sensitive to
enicillin.

Well tolerated at infusion site: Lincocin
intravenous infusions have not
produced local irritation or phlebitis,
when given as recommended. Lincocin
is usually well tolerated in patients who
are hypersensitive to other drugs.
Nevertheless, Lincocin should be used
cautiously in patients with asthma or
significant allergies.

In patients with impaired renal function,
the recommended dose of Lincocin
should be reduced to 25–30% of
the dose for patients with normal
kidney function. Its safety in
pregnant patients and in infants
less than one month of age has
not been established.

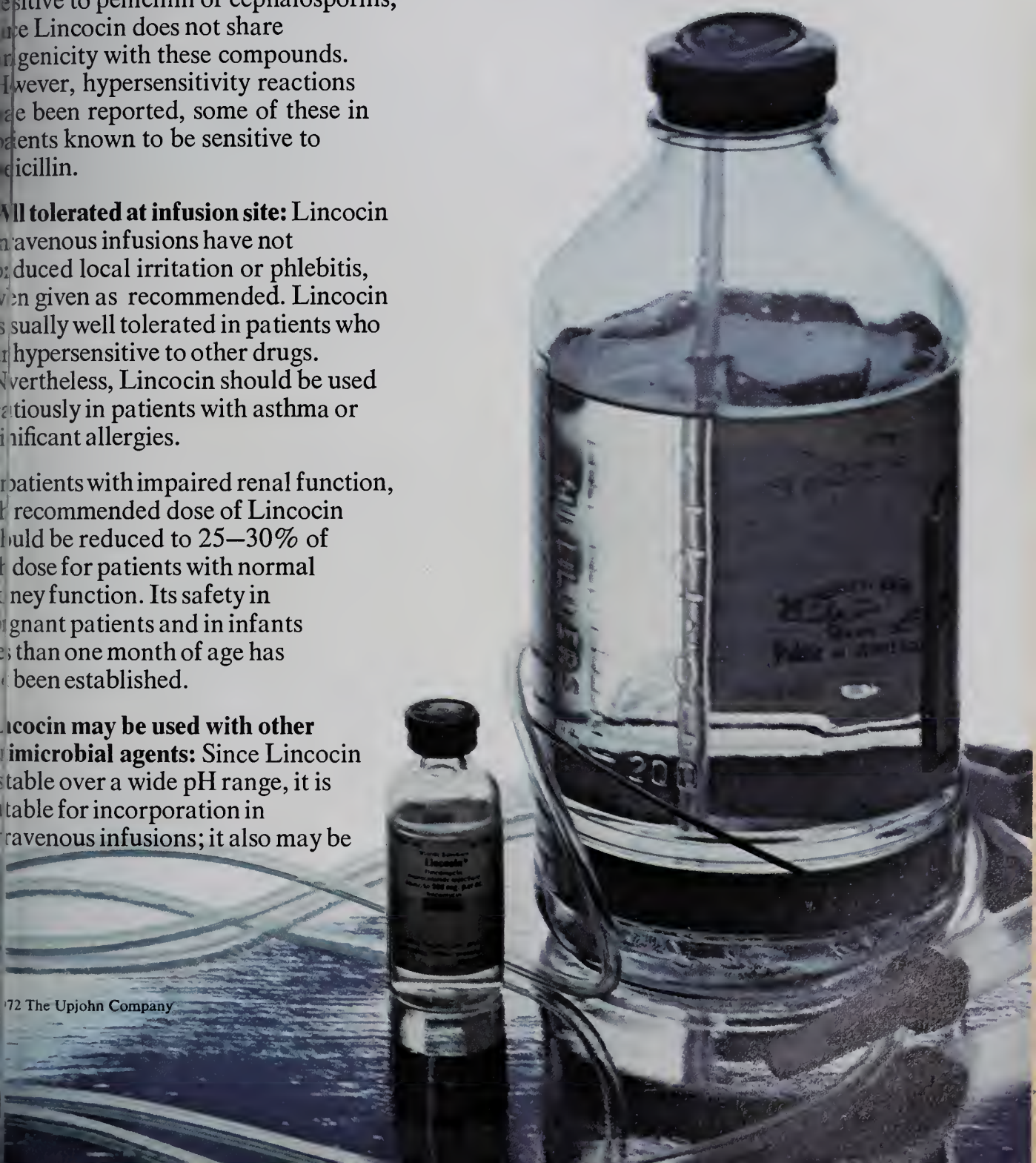
**Lincocin may be used with other
antimicrobial agents:** Since Lincocin
is stable over a wide pH range, it is
compatible for incorporation in
intravenous infusions; it also may be
administered concomitantly with other
antimicrobial agents when indicated.
However, Lincocin should not be used
with erythromycin, as *in vitro* antagonism
has been reported.

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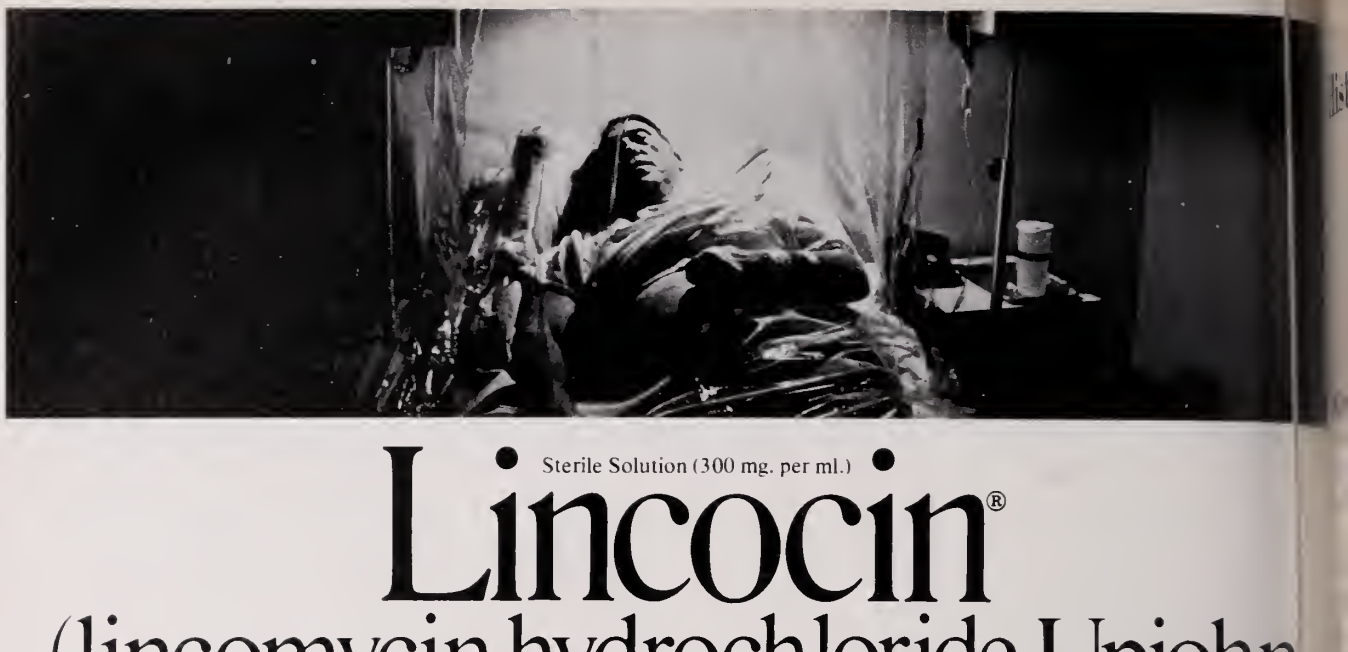
Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more are administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

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Dr. Henry Stanley Plummer
(1874-1936) (Historical Vignette)

THOMAS E. KEYS, M.A., Sc.D. (honorary)

WHEN I CAME to Rochester in 1934, Dr. Henry Plummer (Figure 1) was in his sixtieth year. He often would come up to the library and thus I came to know him fairly well.

At that time I knew little about the many outstanding things he had accomplished for the Mayo Clinic and about his international reputation. But occasionally he took me into his confidence, and would reminisce about his experiences. This physician who pioneered in the study and treatment of thyroid diseases was indeed a genius. He combined great engineering ability with other wonderful attributes, including profound philosophical knowledge. He was able to combine his amazing talents for the good of the institution. Perhaps the people who appreciated him the most were the Drs. Will and Charlie Mayo.

Appearance and Mannerisms

As mentioned by Clapesattle,[1] "Dr. Will Mayo himself said the hiring of Henry Plummer was the best day's work he ever did for the Clinic." Dr. Samuel F. Haines,[2] of the clinic's staff, himself a prominent expert in endocrinology who profited by many years of close association with Dr. Plummer, described him as follows:

"Plummer was tall, spare, and stooped. He had learned to avoid distraction so well that he seemed unapproachable. Thus it was surprising, when he had apparently completely disregarded a question, to have him answer it hours or days later. His ability to become fully absorbed in one subject was so great that he appeared to be unmindful of his associates at times when they wanted him to consider other problems, but it was well recognized by those who worked with him that this same characteristic was responsible for some of his great productiveness. He was a kind and considerate man, willing to devote unlimited time to his patients and to his students."

Because of his powerful concentration he often appeared to be absentminded. Many stories are told about him in this respect. For instance, it is said that he sold his automobile, a Cadillac, to a clinic fellow. But seeing it in the parking lot later, Dr. Plummer drove it home as usual! This obliviousness even extended to his family circle. Mrs. Plummer recalled with a smile meeting her husband face to face one day in a clinic corridor as he strode along to an appointment. His preoccupied expression changed only slightly as he nodded with a formal bow and smile as if to say, "You're someone I must know!" Another story is a typical one. Dr. Plummer invited several of his friends to a luncheon at a hotel in Denver, Colorado, during a meeting of the American Goiter Association. When the check came, he forgot about paying the bill, so one of his friends picked up the tab—but when the waitress brought the change, Dr. Plummer pocketed it.



Fig. 1—Dr. H. S. Plummer in 1936.

Mr. Keys is Senior Library Consultant, Mayo Clinic Library, Rochester, Minnesota.

Unpublished chapter from the College of the Medical Book. The Memoirs of Thomas E. Keys.

See editorial, page 912.

Work on the Esophagus

Dr. Plummer's early work on the esophagus highlights his genius well. As mentioned by Fredrick A. Willius,[3] he made the differential diagnosis between cardiospasm (contraction of the cardiac sphincter) and stricture due to ulceration. His pioneer work on the diagnosis of and treatment for hysterical dysphagia,[4] esophageal stricture,[5] and achalasia[5] was remarkable. The many patients—especially children—who in those days suffered from esophageal stricture due to ingestion of lye or acids were of great concern to him. Frequently ulceration led to complete closure of the esophagus, and the only procedure then available to sustain life was gastrostomy. The usual attempt to dilate the esophageal stricture by forcibly passing bougies from the stomach up through the esophagus often failed. On occasion efforts might be made to cut the stricture. The patient was asked to swallow the end of a silk thread[6] which, if it entered the stomach, could be reached via the gastrostomy opening. A piece of fishline then was attached to the silk thread and drawn up through the esophagus and out through the mouth. By pulling the fishline back and forth from both ends, efforts were made to cut the stricture, but sometimes without benefit.

According to Willius,[3] Dr. Plummer realized the importance of avoiding this type of surgery whenever possible. In 1906 he called attention to the use of silk thread as a guide in procedures for relief of strictures. The patient swallowed six yards of thread, one end of which was retained at the mouth. After as much thread as possible had passed into the intestine, a perforated sound was slipped over the retained end and passed through the mouth and into the esophagus; and with the thread drawn tight, the sound readily entered the stomach. Dr. Plummer designed and made the sounds himself. This form of therapy was safer and easier than gastrostomy and for many patients it was quite sufficient.

Dr. Plummer[5] was also an advocate of the hydrostatic dilator for the treatment of esophageal obstruction and a skillful remover of foreign objects from that organ. He had at home an extensive machine shop for making fine tools and instruments. On some occasions he hurried home from the clinic to make an instrument for a specific patient in critical condition. The instrument would be plated afterward, when the immediate crisis was past.

The First Clinic Building, 1912-1914

As the need arose, the Mayo Clinic added laboratories and equipment.[7] Also when an X-ray machine was procured, Dr. Plummer was placed in charge of this new apparatus. Gradually the laboratories were organized under his supervision.

After a time it became apparent, at least to Dr. Plummer, that a specially designed building was needed to embrace the several units and to coordinate the clinic's practice of medicine. With some persuasion, he got Dr. Will to accept this idea. The first clinic building, which had been formulated in Dr. Plummer's mind for several years, was begun in 1912 and finished in 1914. The prime objective for the new building was to create an efficient system of examination for patients along with necessary laboratories and sufficient storage for case records later to be used in research. In addition, Dr. Plummer felt the importance of creating a harmonious and artistic building. To this end, he went to the famous Rookwood Pottery firm in Cincinnati, Ohio. He described to them his wish for tile to cover the walls of the main lobby and form an entire double stairway. The firm was flabbergasted by such an idea, but before leaving he had convinced them of its feasibility. Though the matching fountain has been removed, that elegant stairway still stands in what is called the 1914 Mayo Clinic Building.

At completion of the clinic building a gala party was held in the main lobby. Dr. Plummer always had an unusually close relationship with the workmen at all levels; and almost to a man the architects, artisans, and laborers who started the project with him were on hand to share in the proud accomplishment of the completed building.

Mechanical Innovations

Dr. Plummer put his mechanical ideas to work. He devised the system of colored lights to indicate the need for special consultants in the diagnostic rooms. He figured out one of the first complete intercommunication telephone systems in the United States. He designed the tube system for sending patients' histories underground from the clinic building to St. Mary's Hospital. These are but a few of his achievements.

The record system itself had been established by Dr. Plummer. Previously each physician had

maintained his own ledger of clinical data, and cross reference for purposes of practice or research was extremely inconvenient. The Mayos wanted these purposes served, and Dr. Plummer based his solution on the radical concept that the clinical data belonged not solely to whichever doctor had recorded them but to the group and should be immediately available to any member. This could be accomplished by a system in which each patient's record was a unit and all units were comprised in a single index, and Dr. Plummer set out to devise one. After much thinking for himself, as mentioned by Dr. L. T. Kurland (unpublished manuscript, 1968), he visited other medical institutions but found no help; so he turned to business and industry for assistance. The system he subsequently evolved and introduced in 1907 became a model for medical records; and even with today's computerization, it is essentially this system that is still maintained. About 1935, when some 60,000 patients were being seen each year, it was necessary to develop a detailed diagnostic and subject cross-index. Miss Mabel Root, a friend of Mrs. Plummer, became the medical record librarian and refined the indexing. When Dr. Joseph Berkson became head of the Section on Medical Statistics in 1933, he saw the value of the Plummer-Root system. Dr. Berkson introduced an automated case-retrieval process, but that is another story.

Interest in the Thyroid Gland

As suggested by Willius[3] in his excellent account, Dr. Plummer's interest in patients with goiter[8] had been aroused in childhood when he accompanied his physician father on calls. One patient seen had an exceedingly large goiter for which Dr. Will Mayo successfully operated.

Following in his father's footsteps, young Henry received his medical degree from Northwestern University in 1898; and he practiced with his father at Racine, Minnesota, not far from Rochester. He joined the Mayo Clinic in 1901 as a member of the permanent staff. About this time Dr. Charles Mayo became interested in the thyroid gland, and from that time for many years operated on the thyroid. Dr. Plummer and Dr. Charlie worked together and wrote a small monograph on the subject which is a classic.[9] Dr. Charlie and Dr. Plummer were responsible for hiring Dr. Edward C. Kendall to head the Section of Biochemistry in 1914 and Dr. Kendall became the discoverer of thyroxin.

But to return to our story. Dr. Plummer made outstanding discoveries in the treatment of thyroid disorders. "His studies on the effect of iodine in the preoperative treatment of exophthalmic goiter . . . led to an immediate reduction of the operative mortality in this disease . . ."[10]

The 1928 Building

Dr. Plummer's medical and scientific achievements have been chronicled by Haines, W. J. Mayo, Willius, and others. The achievement which is his monument is the 1928 Mayo Clinic Building, now called the Plummer Building (Figure 2).

Hardly had the 1914 building been completed when it became evident that more extensive space for facilities would be needed. From that time until the completion of the Plummer Building in 1928, much of Dr. Plummer's time and energy were directed toward this project. A building committee was appointed; but it seldom met, as for practical purposes Dr. Plummer was the committee. He met often with the architects, especially Tom Ellerbe and later Edgar W. Buenger. Much time and effort went into the design of the 1928 building. It is said that when the time had come to excavate, Dr. Will became uncertain as



Fig. 2—The Plummer Building of the Mayo Clinic, completed in 1928.

to the wisdom of undertaking this large project. He consulted with Dr. Plummer about this; but when Dr. Will left the room, Dr. Plummer telephoned the contractor, Mr. Garfield Schwartz: "Get up early and have your men dig a big hole and start the new building."

When Dr. Will saw the excavation he said, "Henry, I guess we might as well go ahead; there is no stopping you, anyway!" And it is said that Dr. Mayo never regretted the decision to go ahead.

This building, which is a work of art, contains features that cannot be replicated. Frank Lloyd Wright said that the clinic library's reading room, first occupied in 1929, was "attractive and commodious"—strong words from Mr. Wright, who was not often complimentary about the work of other architects.

Dr. Plummer anticipated that the library would expand upward and downward. He had an elevator shaft made from the 11th to the 16th floors. When the library was remodeled in 1955, all that was necessary was to add the cab and other equipment. Plummer Hall (on the 14th floor) was converted from a lecture hall to library use in 1968 with little effort, thanks to Dr. Plummer's thinking in 1927 or earlier.

The Browsing Room

Dr. Plummer conceived of the idea of a Browsing Room Library at the clinic for the use of the physicians. He personally selected some 800 nonmedical books, including classics of English and American literature, travel, gardening, exploration, antiquities, and other books covering man's scope of knowledge. He thought that medical men should know of other fields besides medicine. Even if they looked only at the backs of the books, they might learn something. If they devoted a half an hour a day to this nonmedical reading, they would improve their cultural understanding. He realized that men of medicine had little time in medical school and in later training years for this type of reading.

Dr. Plummer also gave me another reason for the Browsing Room. When a fellow or staff member is doing a research project, he tends to get stymied—that is, he runs out of ideas. Dr. Plummer thought that if such a person would come to the Browsing Room and read or browse, he might "click" on how to proceed with his research project.

Artistic Features

Dr. Henry Plummer's fine hand was in everything connected with the Plummer Building. This included the ceilings of the several large waiting rooms. He found an Italian firm, Brioschi and Sons, in St. Paul who were experts in the art of painting artistic ceilings. Mr. Brioschi also designed some of the modeling when he was a patient in the Kahler Hospital with exophthalmic goiter. All of that work is attractive. The elegant ceiling of the 12th-floor Reading Room was executed by Jean K. Kaufmann, now of Fennville, Michigan. Mr. Kaufmann, who received his training in Germany, was also responsible for the ceiling in the old Board of Governor's room. Around the frieze and on the beams of the Reading Room's ceiling are the names of illustrious men and women in medicine and the allied sciences, chosen by Dr. Plummer from his wide reading.

This splendid building is a work of art in Moorish-Gothic style. The finest craftsmen were employed to mould and cast the ornamental bronzes, to sculpture decorations of imported marbles for the interior and exterior, and to paint designs throughout. The building is truly a monument to Dr. Plummer's artistic knowledge and ability, and his responsibility for it is commemorated by a carving set into its outer wall at the first-floor level (Figure 3).

Hobbies

In spite of working prodigiously on both his medical practice and the designing of the clinic building, Dr. Plummer found time for a whole



Fig. 3—Stone inset at southwest corner of the Plummer Building, commemorating Dr. Plummer's design of it.

gmut of hobbies. In his early days at the clinic, fore he married Daisy Berkman, who was a ece of Drs. Will and Charlie, he led numerous mping trips to lakes near Rochester, organizing e whole outing, providing tents for the young en, and setting up all sorts of recreational facili-s, including temporary tennis courts. Some-iat of a gourmand himself, he even planned the od.

Later, for family use, Dr. Plummer had custom-ilt camping equipment. He must have been one Abercrombie and Fitch's best customers, for visits to New York he collected every available mfort for their trips. The wilderness had no lequate accommodations in those days, but with eir deluxe camping equipment, the Plummers joyed touring the national parks and beauty ots of the northern and western parts of the untry and stopping to hunt and fish in some of e choice areas.

Always lovers of nature, the Plummers in the rly days of their marriage owned a country me on Lake Shady at Oronoco with Dr. and Irs. E. Starr Judd. Mrs. Judd also was a niece f the senior Mayos.

The Plummer Cruiser

Soon after giving the Oronoco cottage to the WCA, Dr. Plummer purchased a small cruiser hich was kept at Wabasha on the Mississippi iver. From then on, often with guests, the lummers spent summer weekends on the river. n a trip to New York in the spring of 1936, he ought a larger boat. That summer Dr. and Mrs. lummer initiated the new craft by personally uiding it through inland waters from New York ity to Wabasha, Minnesota. A log kept by Mrs. lummer tells the interesting story of their pass-ng the Statue of Liberty, going up the Hudson nd through the Great Lakes, their experiences on he Marine railways of Canada, with rough waters hrough beautiful Georgian Bay, the stench of the hicago River, the trip through the Illinois River nd canals to the Mississippi, and home base at Wabasha.

The Plummer Home

Earlier, Dr. Plummer had spent countless hours lesigning the English Tudor mansion built on a ill which was then outside the city limits, south of Rochester (Figure 4). Plans for the extensive lawns and flower gardens surrounding the house received much of his attention. In the years when the house was in construction, he studied exhaustively all the books he could gather on the English garden. The resultant landscaping conformed perfectly with the English home, and both Dr. and Mrs. Plummer devoted much time and attention throughout their busy lives to keeping the grounds beautiful.



Fig. 4—Home designed by Dr. Plummer for himself and Mrs. Plummer, which was completed in 1924.

Dr. Plummer Designs a Desk

In 1935 I became reference librarian. On one of his visits to the library, I asked Dr. Plummer if it would be possible for me to have a desk in the Reading Room. He liked the idea and designed a kneehole desk for me, taking into account my proportions. Made by Linden's Glass Company in Chicago from a fine grade of whole matched walnut, in keeping with the other furniture, it is a beautiful piece and is still in the same room.

After Dr. Plummer's death I frequently visited Mrs. Plummer in their beautiful home. Many of Dr. Plummer's books were still in his library. On one occasion I asked Mrs. Plummer whether Dr. Plummer's Baskerville Bible, the elephant folio (1763), was still in his personal library. She said it was, and asked if I would like to have it for the Browsing Room.

I answered, "Yes, we would be delighted to have it."

Mrs. Plummer said, "I'll send my man out with it tomorrow!"

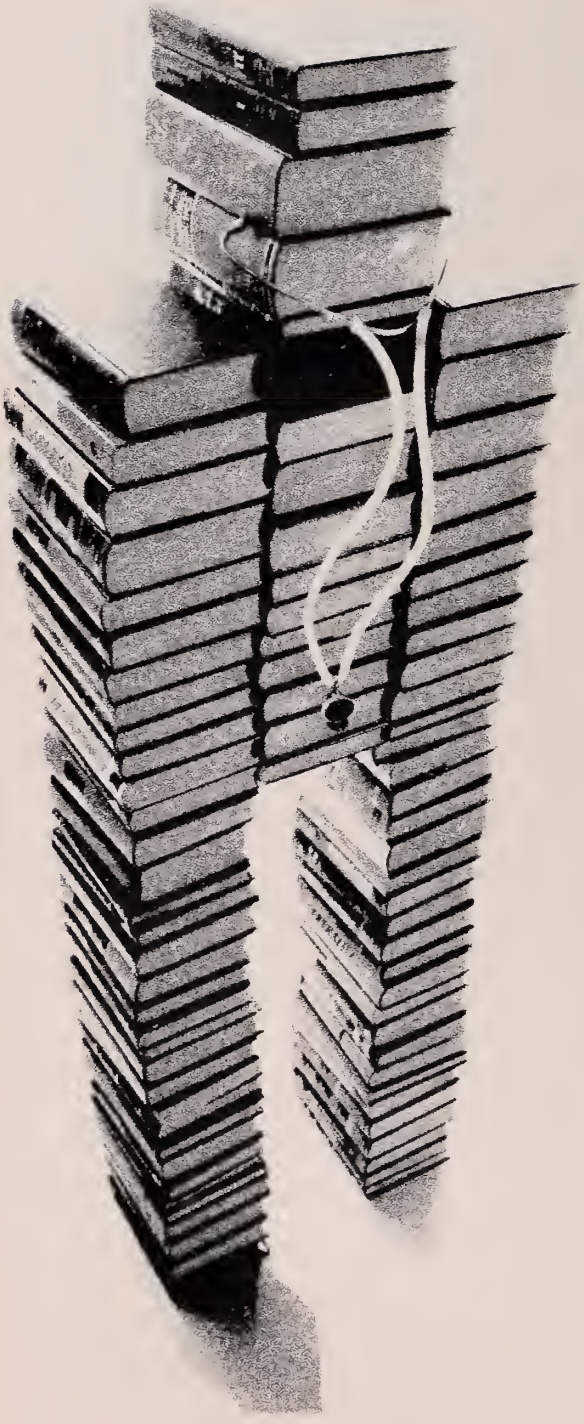
I said, "I'll be your man and take it to the Browsing Room today!"

Acknowledgment

Appreciation is given to Drs. Herman Moersch and Waltman Walters for some of the medical information related in this paper.

References 1-10 will be found on page 963.

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HURRY—Our Wilderness Season extended for 1972. So we can book additional elk and deer hunters. Sept. 15-Nov. 29. Call or write today. John W. McMahon, M.D. 2225 11th Ave., Suite 22, Helena, Mt. 59601. 406-442-0671.

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ORTHOPEDIC SURGEON, certified or board eligible to join a seven man group in Northeastern Iowa. Excellent clinic facilities complete with Xray suites, physical therapy department, and laboratory department. Good hospital facilities available in the area. This is an excellent opportunity for the right man. Partnership after the second year. Contact Mr. George W. Glenn, Business Manager, Waterloo Surgical and Medical Group—319-234-1541.

GENERAL PRACTITIONER to join 2 man group, family practice. Busy, well established location in town of 2000 with drawing area 10,000. Excellent schools, churches, golf club, hunting and fishing, 65 miles from Twin Cities. Completely equipped and staffed clinic. New 40-bed hospital, accredited. Salary arrangements to start and early partnership. Write MINNESOTA MEDICINE, Box 465, 375 Jackson St., St. Paul 55101.

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GENERAL PRACTITIONER—County seat community of 2000. Modern 35 bed hospital 4 blocks from fully equipped clinic. Present associate retiring January 1, 1973. Early partnership. Contact H. A. Knoche, M.D., Gaylord, Minnesota 55334. Telephone 612-237-2528.

ASSOCIATES WANTED: Family doctors to join a growing Family Practice Department in a large multiple specialty medical center, Minneapolis suburb. Excellent opportunity for teaching undergraduate and graduate students in Family Practice. Four man department with excellent growth potential. Reply to Dr. Harley J. Racer, Chairman Family Practice Department, St. Louis Park Medical Center, St. Louis Park, MN 55416. Telephone 612-927-3320.

GENERAL PRACTITIONER to join young 5 man family practice group. College town of 7,000 serving approximately 20,000 population. Accredited hospital with specialist consulting staff. 30 miles from St. Paul-Minneapolis, Minnesota. Contact R. M. Hammer, M.D., River Falls Medical Clinic, River Falls, Wisconsin 54022. Phone (715) 425-5322.

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(Continued to page 966.)

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3 EMERGENCY ROOM Physicians wanted to staff new E.R. facilities of 200 Bed Hospital. 50 man multispecialty Clinic physically adjacent provides immediate consultation and support. No pediatric responsibility. Michigan Resort City on Lake Michigan. Salary negotiable. Many fringe benefits. Reply to: John Rasmussen, Administrator, Burns Clinic Medical Center, P.C., Petoskey, Michigan 49770.

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SENIOR MEDICAL STUDENT seeks employment and learning experience full time from January to June. Particularly interested in orthopedics, surgery, and acute medicine. Jim Haemmerle, 1818 14th Ave. S., Minneapolis 55404.

ST. CLOUD, MINNESOTA—Psychiatrists needed for Psychiatric Service, VA Hospital. Unit System with a variety of therapeutic approaches. Growing Outpatient Service. Fully staffed and newly equipped TV studio and hospital-wide CCTV network available for creative ideas to therapy, education and research. Training affiliations in social work, psychology, nursing, occupational therapy. Three local colleges with many cultural and educational advantages. License in any state accepted. Financial assistance in moving. Liberal vacation, sick and health benefits. Excellent retirement plan. Salary dependent on professional qualifications. Nondiscrimination in employment. Write or phone collect: Chief of Staff, 612-252-1670.

2 ANESTHESIOLOGISTS, (Board Eligible/Certified) wanted to join 2 in 48 man multi-specialty group. Clinic located in Petoskey on Little Traverse Bay in heart of Boyne Country. 7,000 community. Many fringe benefits. Start $32,000. Contact: B. A. Zelt, M.D., Burns Clinic Medical Center, P. C. Petroskey, Michigan 49770.

NORTHFIELD, MINN. GENERAL PRACTITIONER wanted to join busy two-man clinic. No investment. Early partnership. Lab and Xray in office. Excellent hospital. Northfield Physicians and Surgeons, P.A., Bernard Street, M.D. and David C. Halvorson, M.D., Northfield, Minn. 55057.

WANTED—INTERNIST AND GENERAL SURGEON; Board Qualified; for four man group in Iowa; two Internists and two Surgeons; own building; large modern hospital; Midwest shopping and medical center; 30,000; well balanced economy; 2 hours to three large cities; lake resort 10 miles away; hunting and fishing area; excellent school system; Junior college; art gallery; superb library facilities. Salary $25,000 plus bonus, depending on qualification. Early partnership. Write: G. I. Tice, M.D., 121 Third Street N.W., Mason City, Iowa 50401.

MEDICAL SUITE in newer building, approximately 800 sq. ft. Available Nov. 1, 1972. 4200 Cedar Ave., Minneapolis. Ideal location for General Practitioner, joint reception room with dentist's office. Will show after office hours and weekends. Presently occupied by physician. Call 724-9848 or 724-4244. Write Danish American Center, 4200 Cedar Avenue South, Minneapolis.

Book Reports

BONE TUMORS by Louis Lichtenstein, M.D., C. V. Mosby Co., 441 pp, $24.50

Long one of the bookshelf standards in the field of bone tumors, this book has been gradually enlarged and revised, but still resembles the original 1952 edition. The number of illustrations has increased from 155 to 496. There has been scattered updating where indicated and the typography has improved. The book remains small, readily understood, and is enriched with the author's extensive personal experience. The discussion of each type of bone tumor comprises a chapter that starts with historical background and continues with clinical features, roentgenographic findings, pathologic features and treatment. One regrets only that there is not a more detailed discussion of the non-tumorous conditions, such as fibrous dysplasia and the various cysts of bone. The book remains a necessary handbook for all physicians concerned with the diagnosis and treatment of bone tumors.

Robert Woodburn, M.D.
St. Paul, Minnesota

THE CARE OF MINOR HAND INJURIES. 3rd Ed. C. V. Mosby Co. 1972 by Adrian E. Flatt.

Dr. Flatt has superbly created a book for reference for the physician confronted with an injured hand.

The opening chapters dealing with functional anatomy and principles of care are concise, well-illustrated, and free of many extraneous facts and trivia often expounded by hand surgeons which have little, if any, significance to those not completely trained in this exacting field. The remainder of the text deals with specific injuries related to the soft tissues and bones of the hand, and most have been revised to include newer methods of treatment.

The book is well-indexed and the bibliography completed to give the reader easy access to further references regarding a particular topic. This book is highly recommended for anyone treating injuries of the hand and particularly should be available for those who do so only on occasion.

Lee C. Detenbeck, M.D.
Rochester, Minnesota

A PRIMER OF ELECTROCARDIOGRAPHY by George E. Burch and Travis Winsor; 6th Edition, 1972, Lea and Febiger; 292 pages.

These authors published their first edition of this book in 1945. The definition of the word primer, "an elementary textbook," has been nicely adhered to in their presentation of basic principles of this important modality.

The first three chapters cover the theoretical electronic and physiologic phenomena of electrocardiography plus wave form and lead placements. The fourth chapter provides the reader with a concise view of arrhythmias, making certain that the basic physiologic considerations of impulse propagation are well founded in preparation for future rhythm disturbance interpretation. The fifth chapter entitled "Clinical Applications" is short and sketchy in its practical subject materials. It touches briefly on vectorcardiography, though not enough to be of real value to the beginning student.

The book is a virtual carbon copy of the 1966 edition with the addition of his Bundle electrography. It would have benefited from a discussion of some of the new clinical entities and their recently recognized electrocardiographic manifestations—e.g. hypertrophic subaortic stenosis and true high posterior infarction—plus some more specific guidelines on the criteria for diagnosis of cardiac chamber hypertrophy.

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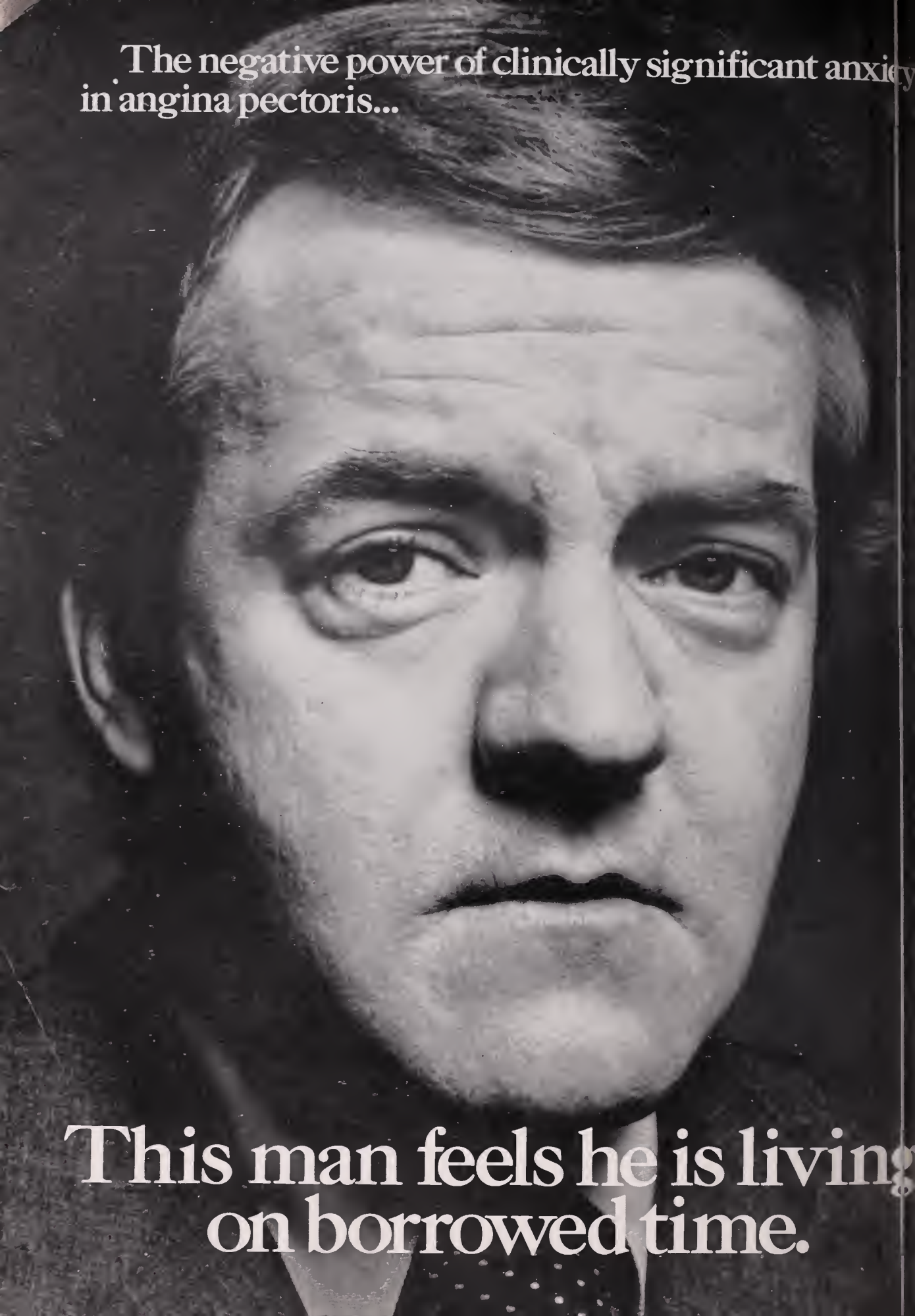


er Song

John P. Wendland, M.D.

NOVEMBER, 1972

The negative power of clinically significant anxiety in angina pectoris...



This man feels he is living on borrowed time.

During anginal attacks, patients may suffer intense apprehension. More frequently, however, they experience a continuing sense of less severe but nonetheless disproportionate anxiety.

Reduction of such clinically significant anxiety is important, since undue emotional stress may precipitate further anginal episodes.

Adjunctive Librium (chlordiazepoxide HCl) may be especially suitable for relief of clinically significant anxiety and emotional tension in anginal patients because of its generally prompt therapeutic effectiveness and wide margin of safety. In a recent double-blind randomized study,* Librium (chlordiazepoxide HCl) was administered for relief of moderate anxiety in 20 anginal patients seen in office practice over a 20-week period. Symptoms of emotional distress related to anxiety were rated at base-line, one week, two weeks and monthly thereafter. Relief was obtained notably early in therapy. The clinical results demonstrated that Librium offers the coronary patient an antianxiety drug that, in the author's opinion, is both effective and safe. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated. (See summary of prescribing information.)

Librium (chlordiazepoxide HCl) is used concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, diuretics and antihypertensive agents, whenever anxiety is clinically significant. The drug should be discontinued after anxiety has been reduced to appropriate levels.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

*Levine, S.: "Angina Pectoris and Emotional Overlay," Scientific Exhibit presented at the Annual Meeting of the Maine Medical Association, Kennebunkport, Me., June 13-15, 1971.

A copy of the Levine study may be obtained from your Roche representative.

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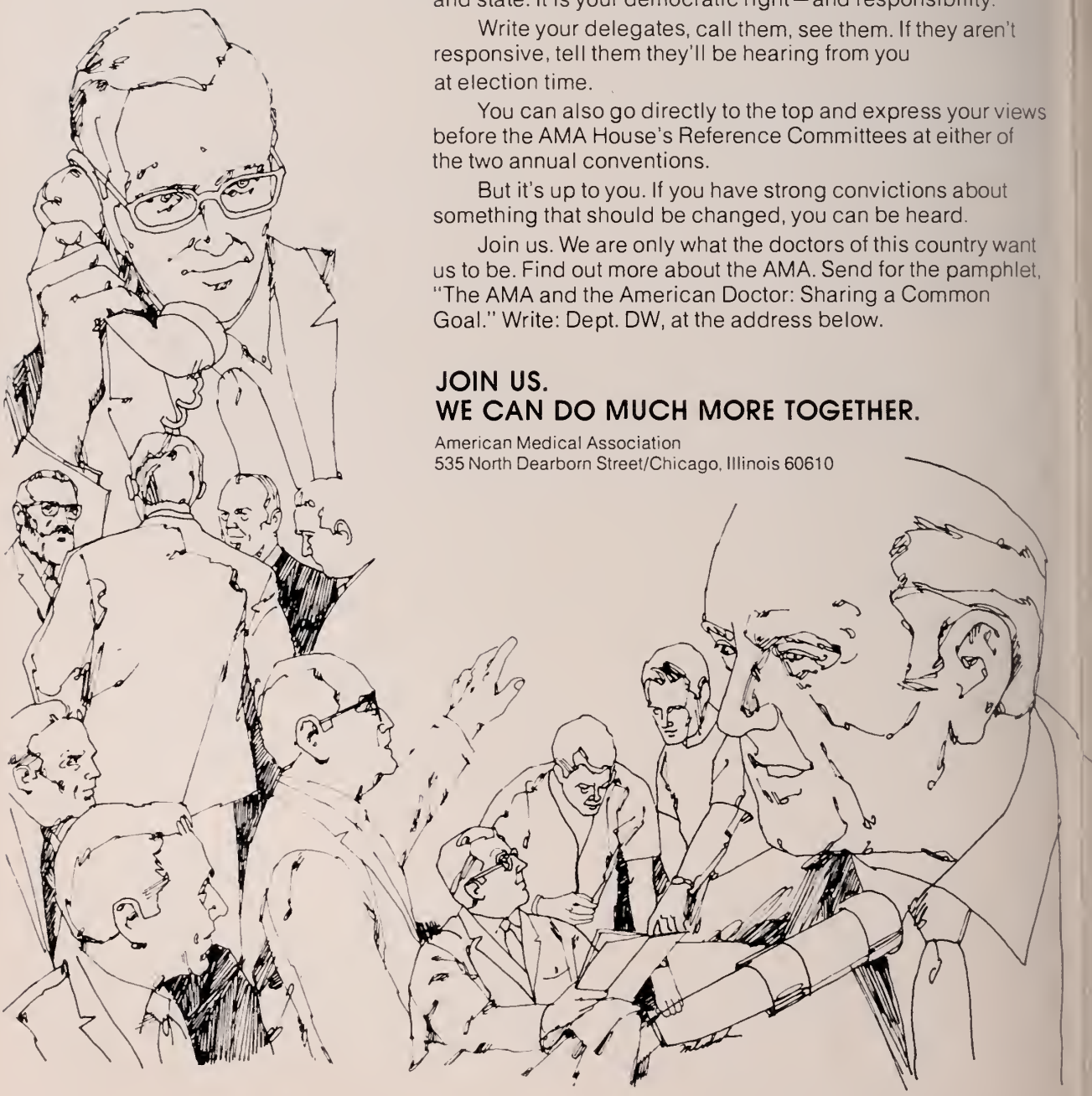
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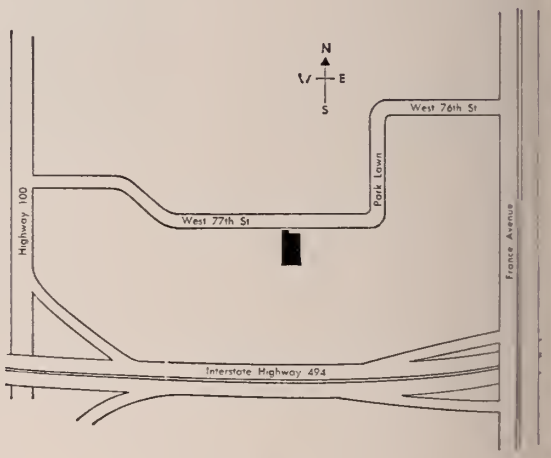
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President's Letter



Freedom from Choice?

EXISTENCE WITHOUT structure is thought to be frightening for the human species. This concept prompted Erich Fromm to author his book Escape from Freedom. November, 1972, finds our country in the midst of either/or confrontations, many of which relate to our political process. Straight ticket voting may be less frequent than ever before, and from what many are saying, some choices for certain offices may not be made at all.

Unfortunately our profession has a high percentage of its members, both young and old, whose philosophy can best be summarized as "I am too busy practicing medicine to be bothered with politics (medical or party);" or "organized medicine, i.e. the establishment, does not represent my views so I will not participate."

To choose to stay outside and exercise your voting right only, to choose not to be involved in your professional society but complain about its posture, is escaping from real choice.

Real choice means a commitment, a risking of yourself and the values you hold as important. You may lose, you may be in the minority, you may find your ideals and values challenged successfully, and this can create an anxiousness most of us would like to avoid. If we can realize selfhood is not dependent on our knowledge, morals or particular ethic, but is due to the fact that *we are,* i.e. a person, a self, then the anxiety of risk taking is lessened. We can then exercise our choices, we can be free to choose real involvement in life.

Physicians are thought of as rugged individualists. If this is so, they are sure of their individualism or if you will, their self. Some I fear are instead rigid individuals who are therefore not sure of self but play the game for their own protection. I hope our profession will become stronger by gaining people sure enough of their selfhood to risk commitment to democratic processes. Will it be said we retreated into freedom from choice? Or shall we go forward to freedom of choice?

George B. Scanlan

President
Minnesota State Medical Association

★

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I certify that the statements made by me above are correct and complete.

REUBEN BERMAN, M.D., Editor-in-Chief

"The history of science, and in particular the history of medicine . . . is . . . the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

– George Sarton, from "The History of Medicine Versus the History of Art"

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion

Results of a questionnaire to 7,000 physicians:

62.9%
Believe combination drug products are useful.

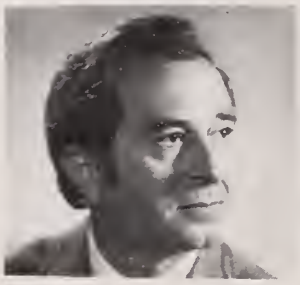
13.8%
Do not believe combination drug products are useful.

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion & Dialogue

Doctor of Medicine

Louis Lasagna, M.D.
Professor and Chairman
Department of
Pharmacology & Toxicology
University of Rochester
School of Medicine
and Dentistry



Obviously, many drugs are given concomitantly. Whether it makes sense to combine medications in one preparation, he it capsule, tablet, or liquid, is a question that can be answered only by examining the advantages and disadvantages in the individual case.

Among the advantages is, first of all, convenience. The more medications that are taken concurrently and the more complicated the diréctions, the less likely tbe patient is to take medications accurately. From the standpoint of convenience and accuracy, and economy as well, you can make an important case for putting medications together in one preparation, as long as they are compatible.

By the same token, when you prescribe a properly tested and rational combination, you should have less worry about pharmaceutical or pharmacological compatibility – and about reasonable dosage ratios as well. Compatibility of the formulation should be demonstrated in the laboratory and clinic before the product is available for prescription—which is more than can usually be said for the physician's own spontaneous creations. And, the dosage ratios employed in rational precompounded combinations are designed to meet the needs of substantial numbers of "typical" patients.

Tbere is no doubt that many "atypical" patients are to he found, and for them the prefahricated comhination must he rejected. But that hardly argues for eliminating rational comhinations from the market. Think, for example, of the problems that would arise if the components of widely accepted combinations, like the oral contraceptives and the diuretic-antihypertensives, always had to he prescribed, purchased and ingested separately.

One disadvantage that comes to mind is some doctors' unawareness of the ingredients a given comhination contains. For example, a doctor might know that a patient is allergic to aspirin hut forget that a certain analgesic mixture, which he knows only hy its trade name, contains aspirin. His prescription, then, causes considerahle discomfort, to say the least. This problem is a function of physician education, rather than of comhination therapy as such. Improving doctors' knowledge ahout all medicaments they prescribe is a problem that deserves tackling on its own.

Another accusation leveled at combination drugs is that they encourage sloppiness of diagnosis and treatment. In many cases, however, a combination may prove to be the most effective choice. A good example of the usefulness of combinations appears in a recent article in the *Journal of Chronic Diseases* on the efficacy and side effects of an antihypertensive containing three ingredients, in which the track records of the combination drug and the individual ingredients were compared. Interestingly enough, whether the drugs were given individually or together, incidence and severity of side effects were the same. But blood pressure control was invariably better when the drugs were taken in one combination tablet than when they were taken separately (in "titratable" dosage) or in two or three different tablets.

Deciding which combinations constitute rational tberapy obviously leads to a discussion of who is to determine which should be used and which should not. Realistically, I think combinations should be evaluated somewhat differently if they are old and established or new and untried.

In today's regulatory atmosphere, there is no possibility of a new combination being put on the market without a subsbantial amount of acceptable evidence in the form of controlled trials that show it to be safe and efficacious. On tbe other hand, I believe a different set of standards should apply to combination preparations that have been around for a long time. In otber words, physician acceptance over a long period should be given some weight as evidence of the efficacy and safety of these drugs.

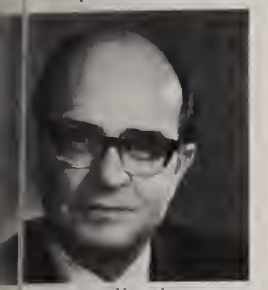
The FDA, however, does not seem to share this attitude. It often requires, for these older products, controlled trials tbat will monopolize the time of already overtired investigators and cost a gre of money. I wisb w agree on a "gran clause" approach t rations tbat have bee for a numher of ye that have an app satisfactory track re

For example, I some of the antibiot hinations that wer off the market by th performed quite we thinking particul penicillin - strepto combinations that —especially surgi tients—were given injection. Tbis ma less discomfort for tient, less dema nurses' time, and opportunities for errors. To take preparation off the doesn't seem to b medicine, unless act age showed a great harm from tbe inj (rather than tbe use) of the combina

The point that sbo emphasized is that are both rational an tional combinations real question is, who determine wbicb is Obviously, the FDA play a major role in ing this determinati fact, I don't think avoid taking the ulti responsibility, but it enlist the help of o physicians and expe assessing the evidenc in making the ultima cision.

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V Clarke Wescoe, M.D.
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combinations generally. Obviously, no one should be exposed willy-nilly to the potential side effects of two or three antibiotics when only one is needed. At the same time there are cases where it is prudent to prescribe more than one. The clinician is the judge in these circumstances, as he should be.

There is no clear definition of the word rational. Most persons, I suppose, would find it synonymous with reasonable, hut in many circumstances it may best he defined as the opinion of those in power at the moment.

Other factors govern combination therapy, not the least of which has been its broad use by practicing physicians anxious to achieve convenience in prescribing, to reduce medication error, and to save money for their patients. Combinations clearly have met the test on all three counts.

I have been impressed by studies showing that the rate of error climbs markedly with the number of medications to he taken, even with sophisticated patients. When medically justified, therefore, this factor alone supports the logic of combination therapy.

The cost argument for combinations appears to be irrefutable. In 1971, R. A. Gosselin studied the 71 combination products (excluding oral contraceptives) among the 200 most prescribed drugs. The study found that if all 71 products were discontinued, and if each ingredient in these combinations were prescribed separately, the price of medicines to patients would jump by $443.2 million on a national basis! At a time when the cost of medical care is under so much fire, it would be nonsensical to boost costs without clearly irrefutable medical reasons.

The part played by government on this question, of course, is fundamental. The FDA should play a role in determining which combinations are reasonable. That role, as defined by law and regulation, is to ensure that any medication on the market is safe and effective in line with its label claims. Certainly combinations are entitled to as much consideration as single entities—neither more nor less. So long as the addition of one drug to another does not make either less safe, or less effective, so long as they are compatible in a formulation, we have a reasonable product. It makes no sense to recommend the use of two products for certain conditions and to deny their being combined in a single form. An unhappy side effect of the problem concerns the efficacy panel discussions of many products submitted for review. The term "effective, hut" has been freely interpreted to mean "ineffective" in toto, regardless of the merit of the individual drugs. This interpretation has placed numerous useful combination products in needless jeopardy.

In reading the actual reports of the review panels, it seems clear that some of the ratings were based less on scientific research and clinical observation than on the "informed" opinions of the panelists. These "informed" opinions were accepted at face value, while the "informed" opinions of others who had used the products were rejected. All of this put combination products into a sort of scientific never-never land.

It should be kept in mind by all, government as well as others involved in our health care system, that advances in therapy are seldom made in leaps and bounds but rather by small painstaking steps—and that some of these steps have resulted from research in combination drugs as well as with single entities. Given the near-infinite biologic variation in patient response, this is hardly surprising to clinicians. It should not be to regulatory agencies either.

In the end, the practicing physician is in the best position to decide if a particular combination makes sense. Such a decision should not be made exclusively by those whose responsibility for continuing clinical care is limited. Clinicians are the best judges of efficacy because the ultimate proof of any product's effectiveness is acceptance by physicians who have observed its actions in patients over time. The corollary statement may he made about over-the-counter medicines, which would not long survive if they failed to afford the relief the user anticipates. That the antihistamine in a "cold" remedy may not *always* be necessary is no reason to proscribe the combination generally.

Opinion & Dialogue

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Snowmobile Fatalities in Minnesota

H. PHIL GROSS, M.D.

THE FIRST SNOWMOBILE built is credited to 'arl Eliason of Saynor, Wisconsin. He put a two nd one half horse out-board motor on a toboggan n the winter of 1924-25 and used it to go hunting nd fishing. Eliason, a Wisconsin storekeeper, atented his machine and sold it to a manufacturng concern that still sells them today.

However, Leo Atherton, a 16-year-old Minneapolis youth mounted a Harley-Davidson motorcycle on a bobsled in 1913 and called the machine a "Sno-Mobile."

There is little doubt that either of these men had any idea of the tremendous popularity their nvented machine would enjoy. It is estimated here are already over one million of these machines in use in the United States, with a projected sales of 350,000 units or more this year. This is still considered minimal saturation of the market; so our statistics concerning injuries and deaths can be expected to increase for several years to come.

Most papers on the subject of snowmobiling have dealt with the injuries involved.[1-7] The site of injury is most often the lower extremity, in a young male. The driver is most often involved, either in a collision with another vehicle, or with a fixed object.

The following case serves to illustrate the narrow margin that exists between a serious "scrape" and death in some snowmobiling injuries.

Case Report

A 14-year-old boy hit a wire restraining rope on a golf course while riding his sno-mobile. Due to irregular terrain, he did not see the wire and sustained a scraping injury of the neck and chin, dislodged his dental braces, and was thrown from the sno-mobile. He was able to remount the vehicle and drive for help.

Shortly afterwards, he was examined and the previously mentioned bruising and scraping were the only obvious injury. He had a full range of motion of the cervical spine and neurological exam was negative.

Dr. Gross is a member of Orthopaedic Associates, Ltd., 1000 South Euclid, Sioux Falls, South Dakota 57105.

Anteroposterior and lateral Xrays of the cervical spine were interpreted as normal. The boy was sent home with instructions for care of skin abrasions which healed satisfactorily. He continued to complain of neck stiffness and returned six weeks later when further Xrays were obtained.

The full extent of the initial injury was then apparent. The subluxation at C2-3 now showed early healing in this altered position. Reduction with fusion was performed.

Three months later the patient's spine was solidly healed, and he was asymptomatic.

Cervical spine injuries in the snowmobile sport do not always terminate so favorably. In Minnesota last year, 16 deaths occurred,[8] of which the largest number were due to head and neck injury.

Fatal Snowmobile Accidents in Minnesota 1970-71	
Head and neck injury	8
Drowning	3
Chest injury	2
Multiple injury	3
	16 deaths



Fig. 1—Lateral view—cervical spine. Taken immediately after injury. No abnormalities seen.



Fig. 2—Anterior-posterior view—cervical spine. Taken immediately after injury. No abnormalities seen.



Fig. 3—Lateral view—cervical spine. Taken six weeks after injury. Show forward subluxation of C2-3.



Fig. 4—Anterior-posterior view—cervical spine. Three months after fusion.



Fig. 5—Lateral view—cervical spine. Three months after fusion.

The multiple injuries listed were a combination of severe head injury, crushed chest, and broken extremity.

This represents an increase in fatalities in Minnesota from 10 the previous year[5] to 16 in the year 70-71. This same trend is seen in the entire United States.

atalities in the U.S.A. Due to Snowmobile Accidents	
54	1968-69
84	1969-70
02	1970-71

Analysis of the 16 Minnesota deaths (14 males and two females) illustrated that the majority of accidents occurred in late afternoon or early evening. The average age was 32 years, with a range from four to 65 years.

New York and Michigan had the highest number of deaths, even though New York had less registered snowmobiles than Minnesota.

State	Deaths	Number of Snowmobiles
New York	18	142,000
Michigan	18	203,411
Minnesota	11	190,000
Wisconsin	6	117,000
Maine	6	43,000
	1969—70	Estimated 1971

While it is possible to count the deaths that have resulted from snowmobile accidents, a reporting system to count the lives saved by the machine has not been devised. While 95% of the machines are sold for recreational purposes, 5% are used for other functions such as law enforcement and various wild life activities. It has allowed penetration of some previously impassible areas in the winter-time. Two years ago when our area had an unprecedented large snowfall, it helped distribute food and medication to many stranded people.

From the reports reviewed, there are two factors which have a direct relationship with the fatality: speed and visibility.

Speed and visibility are closely linked, because the faster the vehicle is moving, the less reaction time is present to respond to what is visible. Although the usual speed of the snowmobile is 15-35 miles per hours, speeds exceed 100 miles per hour in racing. The newer models have increased horse power, and travel at 50 miles per hour is not unusual.

After review of the accidents and fatalities that have occurred, the following recommendations are listed.

Driver:

1. **Become familiar with your machine.**
2. **Become familiar with the terrain.**
3. **Be aware of unsafe weather conditions.**
4. **Do not explore unknown territory at night.**
5. **Do not "jump" the machine with more than one person on board.**
6. **Do not follow other vehicles too closely.**
7. **Tow only with a solid tow bar.**
8. **Wear proper attire.**
   a) **No loose clothing that can catch in gear.**
   b) **Wear helmet and goggles.**
   c) **Wear weather-proof suit. (There is one available that will keep you afloat.)**

Manufacturer:

1. **Develop an unbreakable windshield that will protect the head, face and neck.**
2. **Supply proper lighting.**
3. **Supply proper leg protection.**
4. **Supply a dead-man's* throttle that will not stick.**
5. **Continue research regarding proper ski width, suspension, and angle of attack on snow, plus better traction for control of the machine.**

*"Dead-man's" throttle is that type of throttle that will bring the machine to an idle the minute the hand is released.

Summary

A case of a cervical spine injury while snowmobiling is presented and the subject of head and neck injuries and snowmobile fatalities is reviewed. Safety suggestions for the driver and manufacturer of snowmobiles are outlined.

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After all there is but one race—humanity.—George Moore

Malignancy in A Longstanding Colon Polyp

JAMES J. MONGE', M.D.

THE MALIGNANT POTENTIAL of adenomatous polyps of the colon is still considered controversial. Castleman[1] has stated that the probability of carcinoma arising in such a polyp is negligible. The following case is relevant.

Case Report

An obese 82-year-old man was admitted to the hospital for treatment of emphysema, myocardial ischemia with congestive heart failure and bronchopneumonia. After the patient's condition had improved surgical consultation was requested because of a tumor of the colon.

A polyp 3.5 cm. in diameter had been found in the hepatic flexure of the colon by barium enema examination seven and one-half years prior to this hospitalization (Figure 1). Because of his age and fragile general health the patient's physician had not recommended surgical excision of the polyp. A barium enema examination two years later showed the polyp unchanged in form and size, but radiologic examination four years after discovery showed the polyp to have enlarged to 5 cm. in diameter. Over the next two years no further change in the size was seen on annual Xrays, but the most recent barium enema, performed during the present hospitalization, demonstrated an annular carcinoma of the colon at the exact site of the previously seen polypoid tumor (Figures 2 and 3).

Laparotomy confirmed the presence of an adenocarcinoma of the right colon with a large metastasis in the central portion of the liver. A palliative right hemicolectomy was performed. The ulcerated tumor measured four cm. in length and involved the full circumference of the colon. No other polyps were found.

The patient returned home but later developed cachexia, hepatomegaly, and icterus, and expired five months after operation.

Pulmonary and adrenal metastases were found on necropsy examination. The liver, in addition to a large central mass of tumor measuring 13 X 10 X 10 cm., was diffusely involved with nodules of metastatic carcinoma measuring up to 2.5 cm. in diameter. An acute duodenal ulcer, bilateral pyelonephritis, coronary atherosclerosis with myocardial scarring, pulmonary emphysema, and severe bronchopneumonia were also found.

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See editorial, page 1014.



Fig. 1—Initial barium enema examination showing a large polyp in the hepatic flexure of the colon, seven and one-half years prior to right hemicolectomy.

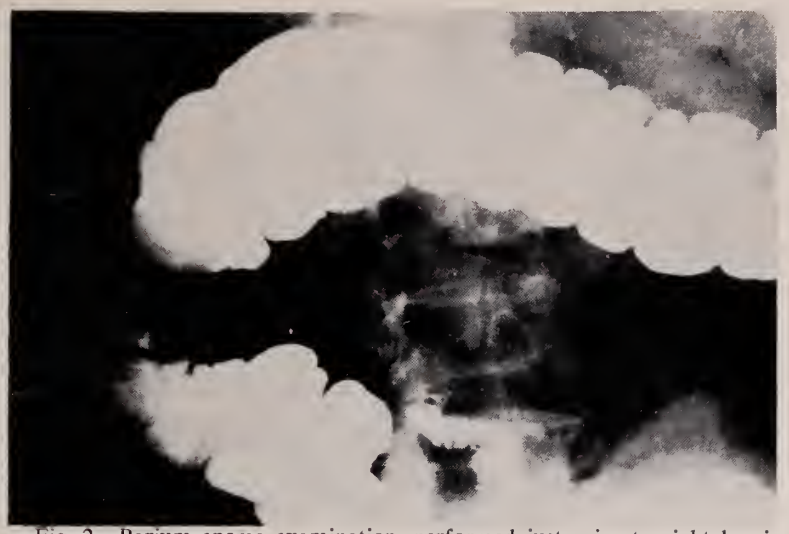


Fig. 2—Barium enema examination, performed just prior to right hemicolectomy, demonstrating an annular adenocarcinoma of the colon at the site of the polyp shown in Figure 1.

Comment

At least 18 case reports have been published in which patients, within two to 19 years, have developed carcinoma at the site of a previously demonstrated, but not removed, colon polyp.[2] It has also been shown that carcinoma arising in the tip of an adenoma can be an early anatomical stage of clinical cancer; in at least 14 instances cited, lymph node, hepatic or pulmonary metastases have been associated with such a lesion.[3,4]



Fig. 3—Spot film of the annular adenocarcinoma of the colon.

The tumor found in this case enlarged very slowly during the first six years that it was followed, only doubling in size while retaining a polypoid appearance. Rapid growth during the year prior to surgery culminated in an obvious annular carcinoma. One may postulate that the tumor was a slow growing adenocarcinoma from its inception. On the other hand, the abrupt change in growth rate and appearance suggests that this was a benign polyp of the colon that became malignant.

Many adenocarcinomas of the colon may arise *de novo* from the mucosa or from villous polyps. However, since small polypoid carcinomas cannot be differentiated radiographically from benign polyps, and since adenomatous polyps may become cancerous, the surgeons at the Clinic continue to recommend removal of polyps of the colon which are sessile or are greater than 1.5 cm. in diameter (as well as all those within reach of the proctoscope). The polyp is oriented for central perpendicular sectioning; if frozen section examination discloses invasive carcinoma, a bowel resection is performed.

See references, page 990.

Congenital Coronary Arterial Venous Fistula

Repair

JOSEPH C. KISER, M.D. AND ROBERT SCHULTZ, M.D.

SINCE FIRST DESCRIBED by Drause in 1885, congenital fistula of the coronary arteries has been reported nearly 200 times. The fistula is most commonly between the right coronary artery and the right heart. Rarely the left coronary artery and the left ventricle are involved. A variety of surgical procedures have been described for treatment of this lesion. Although the methods of treatment previously described have met with varying degrees of success, we believe that total excision of the fistula and repair using a vein graft from the aorta to the distal normal coronary involved represents a new and better method of treatment. The following is a case report of a congenital fistula of the right coronary artery communicating with the pulmonary artery, coronary sinus and right ventricle.

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Case Report

This 35-year-old-white female was initially noted have a continuous murmur in the left second interspa on a routine obstetrical visit. She was asymptomatic. was the impression of the consulting cardiologist that th represented a patent ductus arteriosus without seve hemodynamic derangement. Her blood pressure w 120/80. The first and second heart sounds were norm There was a continuous murmur which was accentuate just prior to the second heart sound and advanced int the early part of diastole. It was believed to be a typic patent ductus murmur in both its location and intensit A thoracic aortogram was obtained which revealed small tortuous patent ductus arising from the inner borde of the distal aortic arch. The electrocardiogram wa normal. On May 3, 1971 the patent ductus was divide through a posteriolateral thoracotomy. It was approx mately four mm. in diameter, long and tortuous. Afte dividing the patent ductus, it was noted that the contin uous thrill over the pulmonary artery was still present The pericardium was opened. A markedly enlarged an tortuous right coronary artery was found. The thrill wa

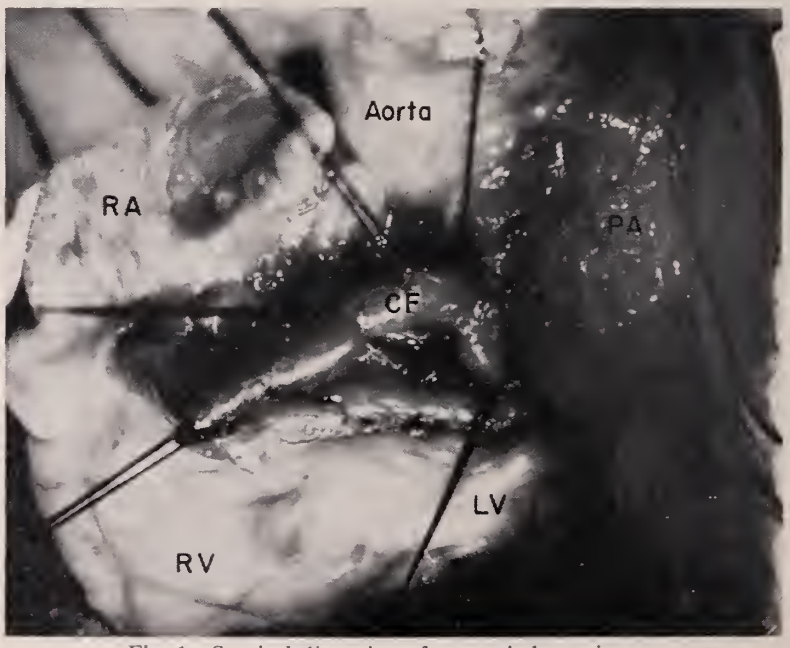


Fig. 1—Surgical dissection of congenital arteriovenous fistula. CF—arteriovenous fistula involving right coronary system. PA—pulmonary artery. RV—right ventricle, LV—left ventricle. Connection of fistula with aorta is rudimentary.

noted to be most intense at the root of the main pulmonary artery. The chest was closed in the usual fashion and her postoperative course was uncomplicated. On May 7 a selective coronary angiogram was obtained. The left coronary demonstrated an extremely large left common with a large tortuous left anterior descending, left circumflex and left marginal branches. There was an extensive anastomotic network from the circumflex to the marginal branches which filled the tortuous and aneurysmal right coronary artery retrograde. The proximal end drained into the pulmonary artery and coronary sinus. No right coronary ostium was present in the right aortic sinus. The left ventricular end diastolic pressure was slightly elevated. The conclusion of this study was that there was a large left coronary artery with collateral filling of the entire right coronary artery via the left marginal and circumflex branches. The anomalous origin of the right coronary artery was from the pulmonary artery. She was discharged from the hospital and re-admitted on June 29, 1971. At that time, her heart was explored through a median sternotomy. Extracorporeal circulation was employed. When the heart was examined, there was noted to be a continuous thrill over the main pulmonary artery. There was a large caliber tortuous thin walled structure occupying the right atrioventricular sulcus. It appeared to arise from the root of the pulmonary artery. There was a rudimentary connection with the root of the aorta. The right coronary artery was completely dissected and 00 silk ligatures were passed around all branches to the right coronary artery down to the junction of this vessel with the posterior-descending coronary artery. These vessels were dilated, tortuous and thin walled. It was obvious that the flow was in a retrograde manner through the fistulous vessel into the pulmonary artery. After completely dissecting this vessel (Figure 1), we were convinced that the entire right system filled from the left coronary artery by way of the posterior descending into the right main coronary artery since there was a large left to right shunt present. After exposing all branches of this fistula, it was excised and the individual branches ligated. The main entrance point into the pulmonary artery was also ligated. From the anatomic appearance of this anomalous vessel, it was entirely possible that there were multiple communications with other chambers of the heart. After the anomalous vessel had been completely dissected free and its branches ligated, a saphenous vein graft was utilized to reconstruct the right coronary system (Figure 2). The proximal anastomosis was made to the ascending aorta and distally the vein graft was anastomosed to the posterior descending coronary artery. Bypass was gradually discontinued and hemodynamics were immediately satisfactory. Flow was measured in the saphenous vein graft and it was found to be 50 cc. per min. Her postoperative course was uncomplicated and she was discharged from the hospital on the ninth postoperative day. She has remained asymptomatic.

Discussion

The diagnosis of coronary artery fistula may be somewhat difficult clinically particularly when the main fistula drains into the pulmonary artery. As in this case, the clinical findings are indistinguishable from patent ductus arteriosus. Indeed, approximately 20 percent of patients with coronary artery fistula have other cardiac anomalies.[1] In

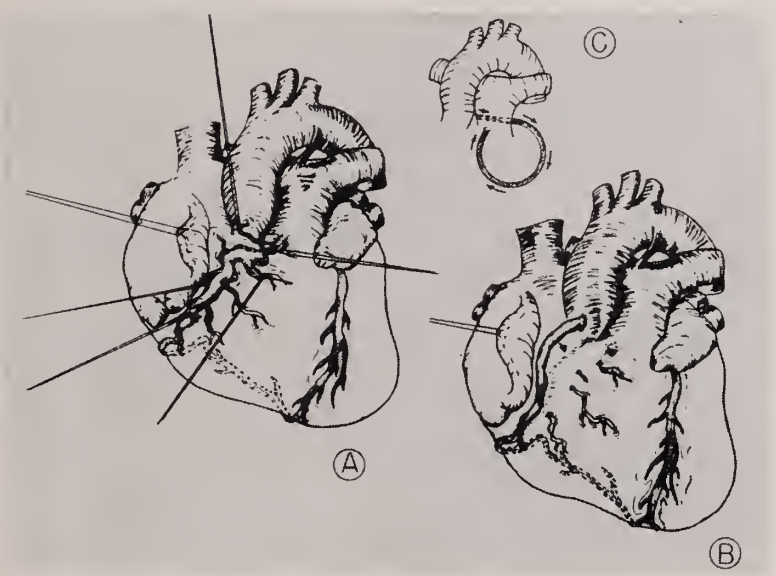


Fig. 2—Diagramatic sketches of a congenital coronary arteriovenous fistula and its repair. (A) Large fistula of right coronary system connecting with the posterior descending coronary artery and draining into the main pulmonary artery. (B) Excision of the fistula and reconstruction of the right coronary arterial system by anastomosing a saphenous vein graft between the posterior descending branch of the right coronary artery and the aorta. (C) Diagram indicating the left to right shunt between the left coronary artery and the pulmonary artery via the coronary arteriovenous fistula.

the adult variety of the lesion, patent ductus is the most common associated malformation. Depending upon which chamber the fistula enters, the location of the murmur may be atypical for patent ductus arteriosus. Although myocardial ischemia associated with this lesion is an uncommon feature, occasionally myocardial necrosis has followed simple ligation of the fistula. The majority of these patients with the adult form of the disease are symptomatic. Bacterial endocarditis has been noted to occur in 10 percent and may be the first clue to the anomaly. Although the aneurysm is an extremely thin walled vessel, spontaneous rupture has been rare. Derangement of hemodynamics varies according to the volume of the left to right shunt. Chest Xray is not diagnostic although a few unusual cardiac silhouettes have been reported due to aneurysmal dilatation of the involved coronary. Electrocardiography has not proved helpful in isolating these cases. Probably the greatest advance in localizing the lesion is the result of refinement in technique of coronary angiography in recent years. A number of surgical approaches have been suggested for treatment of coronary artery fistula. Biorck and Crafoord[2] in 1947 successfully closed a fistula by ligating the involved artery. Since that time, a number of patients have been treated in this manner. On occasion, this has resulted in distal ischemia and myocardial necrosis. It has become apparent that preserving the continuity of the coronary artery or coronary fistula and its distal blood supply is important. In 1962, Cooley[3] employed interlocking mattress sutures behind the coronary artery to accomplish this. However, recurrent fistula formation has been reported using both of these techniques. More recently, Gross and McNamara[1] in 1968 favored closure of the fistula through a ventriculotomy. Each of these techniques has the disadvantage of leaving an abnormal thin walled vessel in place which carries the risk of rupture and recurrence of the fistula. Indeed, thrombosis and late rupture have been reported following the ligation procedure. Although the literature is not clear on the possibility of multiple points of communication with the various chambers of the heart, it would appear from review and from our case that multiple communications with the various chambers may occur. For these reasons, we believe that total excision of the anomalous vessel and reconstruction using a vein graft from the aorta to the distal normal portion of the involved coronary system is an improved method for dealing with this problem.

Summary

Coronary artery fistula is an uncommon congenital cardiac malformation. Advances in coronary angiography as well as vein by-pass techniques which have been used in treating other types of coronary artery lesions make it possible to treat coronary artery fistula by total excision and reconstruction using a vein graft. Recurrence of the fistula following this procedure is unlikely. It also affords re-establishment of a double coronary artery circulation in a nearly normal pathway.

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Ne can my counsel yet withdraw the heat
*And furious pangs of his inflamed head.**

*Thomas Norton & Thomas Sackville: Gorboduc, III.i.35-36. 1562

Permanent Transvenous Sequential Atrioventricular Pacing

Problems in Its Application

AMADO S. SANTOS, M.D., MARTIN WYNYARD, M.D. AND MARTIN M. BLACK, M.D.

PERMANENT TRANSVENOUS sequential atrioventricular (A-V) pacing requires a safe, simple and stable atrial electrode. American Optical Corporation's J-shaped electrode best fulfills these criteria (Figure 1).

The following case report illustrates the successful use of such a pacer where a temporary ventricular demand pacer proved to be a failure. The pacer used was a bifocal atrioventricular demand type from the American Optical Corporation. It consists of two units in a single package, (Figure 2): A conventional QRS inhibited ventricular pacer and a QRS inhibited atrial pacer which share a single QRS detector. To understand its mechanism two terminologies require clarification: Atrial escape interval and ventricular escape interval. Both intervals are timed from either a sensed or an induced R wave (Figure 3).

If the patient's normal R-R wave interval is shorter than the pacer's atrial escape interval, the pacer will be totally dormant. If the patient's normal R-R wave interval is longer than the pacer's atrial escape interval, but shorter than the pacer's ventricular escape interval, the pacer will stimulate the atria and be inhibited in the ven-

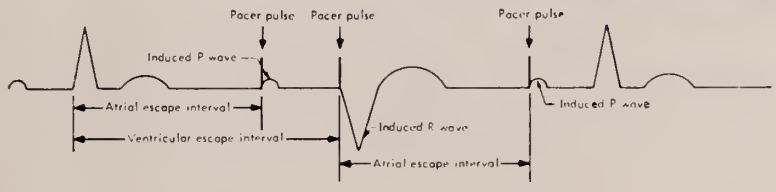
Dr. Santos is Associate Attending, Medicine;
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Dr. Black is Attending and Chairman, Department of Medicine, Community General Hospital, Syracuse, New York.



Fig. 1—J-shaped atrial electrode. Tip diameter and body diameter 10 French.



Fig. 2—Bifocal demand pacemaker.



Animation of AV escape interval relationships

Fig. 3—Self-explanatory.

tricles. If the patient's normal R-R wave interval is longer than the pacer's ventricular escape interval, the pacer will stimulate both the atria and the ventricles in sequence.

Techniques Involved:

1. Local anesthesia with the anesthesia department in standby.
2. Atrial electrode hooked into the right atrial appendage preferentially with the tip turned to the right (Figure 4).
3. EKG monitoring with a battery operated unit which is directly connected to the endocardial electrodes during positioning.

Case Report

An 80-year-old woman admitted to the hospital in September, 1971, with an acute anterior myocardial infarction and whose hospital course was complicated by various arrhythmias as well as a refractory congestive heart failure.

The patient has been a diabetic for 15 years. She has had severe hypertension in the past. Six years ago she was found to have splenomegaly. In 1970 the spleen became massively enlarged associated with hypersplenism, pleural effusion, and massive ascites. A splenoportogram was normal. The ascitic fluid was evacuated by cannulation of the peritoneal cavity and drainage into an apparatus allowing direct retransfusion into the venous system (a total of 23 bags in four days were thus autotransfused). She developed multifocal atrial tachycardia, sinus bradycardia, junctional (A-V) rhythms and other types of arrhythmias. In spite of pharmacological agents the bradycardia persisted. A temporary pervenous ventricular demand pacer had to be inserted prior to a successful splenectomy (1380 gm) and an abrasion hepatopexy in November, 1970. The patient did well after surgery and was sent home in December, 1970, without a pacer.

Physical examination on the present admission showed normal vital signs. The neck veins were flat, the lungs clear, and the heart rate was 100 per minute with frequent extrasystoles. No murmur or gallop was heard. There was no ascites, hepatomegaly, or pedal edema.

The initial electrocardiogram showed sinus rhythm at 100 per minute, normal A-V conduction, complete right bundle branch block, few P.V.C.'s and deep Q waves with S-T elevation in V1 to V4 consistent with an acute anterior myocardial infarction. Soon after admission to

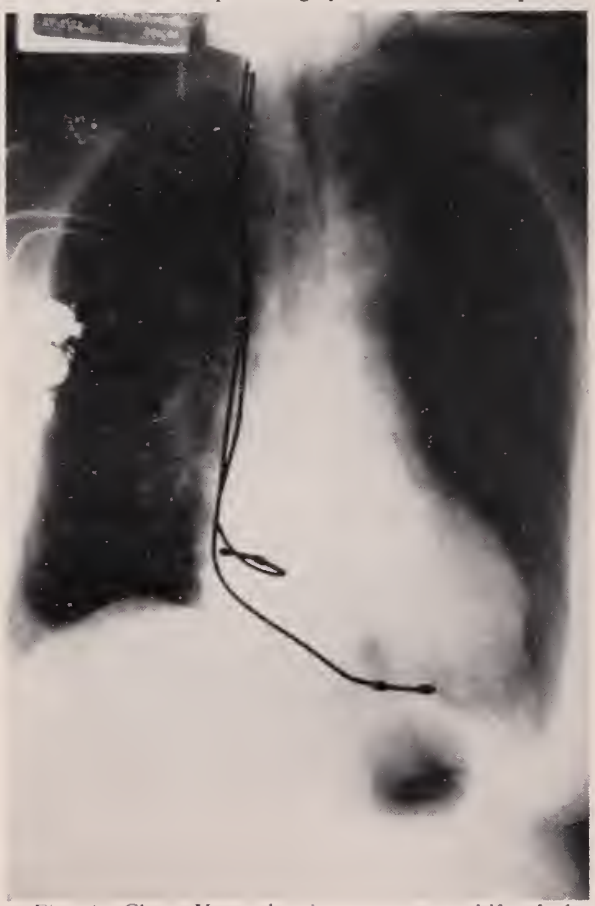


Fig. 4—Chest Xray showing permanent bifocal demand pacemaker and electrodes after implantation. Note tip of atrial electrode pointing to the right. The electrodes are re-touched to achieve contrast. Considerable clearing of lung fields when compared with ventricular pacing alone (Figure 6).



Fig. 5—Right lateral chest film after implantation of permanent bifocal demand pacemaker. (Electrodes retouched.)

the coronary care unit the patient developed runs of ventricular tachycardia which responded to Lidocaine. Two days later she developed supraventricular tachycardia which changed to sinus bradycardia and atrial standstill after parenteral Digoxin. The patient's condition deteriorated rapidly. A temporary pervenous ventricular demand pacemaker was inserted in September, 1971. The patient continued to have various arrhythmias including supraventricular tachycardia, junctional (A-V) rhythm and refractory congestive heart failure in spite of pharmacologic agents. (Figure 6). In November, 1971, a permanent transvenous sequential A-V pacer replaced the ventricular pacer. (Figures 4 and 5). The patient gradually diuresed and improved clinically.



Fig. 6—Chest Xray prior to sequential pacing showing temporary transvenous ventricular electrode. (Electrode re-touched.) Passed via a left superior vena cava remnant through the oblique vein of the heart into the coronary sinus. Note persistent pulmonary congestion.

Comment

Atrioventricular pacing has certain physiologic advantages in specific clinical settings over ventricular pacing. With A-V pacing the atrial contribution to the ventricular end diastolic volume is retained. Studies have shown that sequential A-V pacing can augment the cardiac output by as much as 24% and that arterial pressure rises while venous pressure falls. In demand sequential atrioventricular pacing the machine senses the ventricular endocardial electrogram and paces the atrium and ventricle sequentially, (Figure 7). A comparison of the various types of A-V pacing is shown in the Table.

With the use of a J-shaped atrial electrode positioned in the right atrial appendage, reliable permanent pacing with a transvenous electrode is now available. (Turning the tip of the electrode

TABLE

DIFFERENCE BETWEEN THREE MODALITIES OF A-V PACING

P-wave Triggered	A-V Sequential-Continuous	Bifocal Demand or A-V Sequential-QRS Inhibited
Monitors P-waves	No Monitoring	Monitors QRS Complexes
P-waves Control Ventricular Stimulation no Atrial Stimulation Available	Stimulation is Not Affected by the Intrinsic Cardiac Activity	QRS Complexes Control Both Atrial and Ventricular Stimulation
Stimulation is Delivered to the Ventricles Continuously	Stimulation is Delivered Both to the Atria and Ventricles Continuously	Stimulation May Be: a. Totally Absent b. Delivered only to the Atria c. Delivered both to the Atria and Ventricles
Useful for A-V Block With Normal Atrial Activity	Used Mainly for Temporary Pacing	Useful for Atrial Bradycardia With Intermittent A-V Block

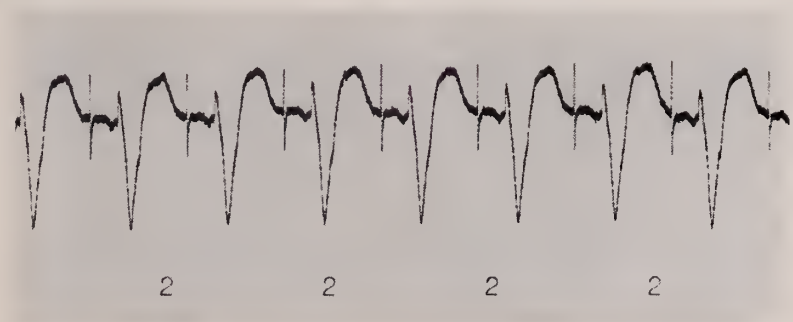


Fig. 7—EKG tracing with bifocal demand pacemaker during A-V sequential stimulation.

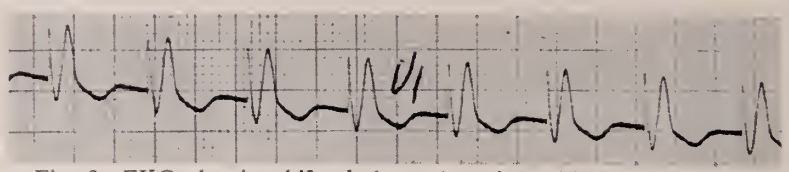


Fig. 8—EKG showing bifocal demand pacing with junctional (nodal) rhythm. Note pacer's spontaneous atrial spike closely preceding QRS. There is no ventricular pacer spike.

to the right appears to increase the stability of the electrode.) In this particular case with a sinus bradycardia we were able to set the pacer rate at a more economical level of 85 per minute. Although we did not measure the cardiac output, the patient's clinical condition including the previously refractory congestive heart failure which developed when a temporary ventricular demand pacer was in place, improved significantly after the insertion of the permanent sequential AV pacer.

An interesting diagnostic tachycardia developed two weeks after the A-V pacer was implanted (Figure 8). The questions of endocardial electrode displacement or pacer failure were ruled out by chest Xray and by activating the pacer's reed switch with an external magnet respectively. With a very short interval of 0.04 seconds between the pacer atrial spike and the succeeding QRS the possibility of accelerated A-V conduction was considered. However, the pattern is best explained by nodal (A-V) rhythm with the patient's own R-R wave interval (0.5 seconds) just slightly longer than the pacer's atrial escape interval (0.46 seconds) but shorter than the pacer's ventricular escape interval (0.71 seconds). Therefore, each QRS is followed by an atrial pacer spike 0.46 seconds later. The patient reverted spontaneously to sequential pacing after two hours.

Although the follow-up on this single case is not adequate to establish its longterm value, we have shown in this instance sequential A-V pacing did improve cardiac function from that accomplished by ventricular pacing alone.

Summary

The successful use of a permanent sequential A-V pacer in a patient with refractory congestive heart failure and rhythm disturbances where a previous temporary ventricular pacer failed, and technical points in electrode placement and interpretation of an apparent abnormal pacing sequence were discussed.

Acknowledgment

We would like to express our sincere appreciation to Mr. Jason A. Sholder, Manager of Pacemaker Products, Medical Division, American Optical Corporation for his help in the insertion of this pacemaker and the suggestion for atrial electrode placement.

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A taste for drink combined with gout,

Had doubled him up for ever.

Of that there is no manner of doubt—

No probable, possible shadow of doubt—

*No possible doubt whatever.**

---

*W. S. Gilbert, "Don Alhambra's Song," The Gondoliers, 1889.

The Flora and Fauna of Hernial Sacs

A Plea for Routine Histologic Examination

LUIS H. TOLEDO-PEREYRA, M.D. AND PATRICK C. J. WARD, M.D.

A NUMBER OF ABDOMINAL and pelvic organs occasionally find their way into hernial sacs. These include bladder, appendix, tubes and ovaries.[5] Two cases of ectopic pregnancy have now been reported in such a setting.[5,22] Occasionally, unsuspected cancer may be discovered on gross or microscopic examination of a hernial sac.[8] Splenic tissue is also intermittently found in scrotal hernias,[23] and in this location represents either continuous or discontinuous splenogonadal fusion. This anomaly apparently occurs only on the left side.[19,23] Rarely, endometriosis may present for the first time in hernial sacs.[17,18] Finally, the occurrence of adrenal rests in the hernial sacs of children, although frequently noted at surgery, has been only occasionally documented.[9,10]

Because of the low yield of significant pathology in hernial sac tissue, pathologists in some instances limit examination of the surgically removed hernial sac wall to documentation by measurement and cursory macroscopic description. Over a period of 16 months at Mount Sinai Hospital, Minneapolis, a 300 bed general hospital, histologic examination of 212 consecutive hernial sacs yielded three instances of disease or ectopia, all of which were unsuspected prior to surgery and two of which were unsuspected even on gross examination.

Case Reports

Case 1

A three-month-old boy was admitted for repair of bilateral inguinal herniae. A hydrocele had been noted on the right at birth. Subsequently, an intermittent fullness of the sac suggested patency of the processus vaginalis. Shortly before admission, a hernia developed above the hydrocele in the right inguinal canal. A hernia was also noted on the left side. The pre-operative diagnosis was bilateral indirect inguinal herniae with communicating hydrocele on the right. In August, 1970, a bilateral inguinal herniorrhaphy and right hydrocelectomy were performed. While grossly unremarkable, the hernial sacs were routinely sectioned and a thin, cord-like spleen, 1.8 x 0.4 x 0.3 cm. was found on the left side (Figure 1). No testicular tissue was noted histologically. The postoperative phase was unremarkable.

Case 2

A 23-year-old woman was admitted for repair of a suprapubic ventral hernia. The patient had a history of two previous Caesareans done through a Pfannenstiel incision and for the five or six months prior to admission had had pain and a mass in the midline of the lower abdomen. The pre-operative diagnosis was ventral hernia. At surgery incarcerated omental tissue was found in the hernia which was in the line of previous incisions. This was excised and the defect in the fascia repaired by a Mayo procedure. Microscopic examination of the hernia sac revealed mural endometriosis (Figure 2). The patient's

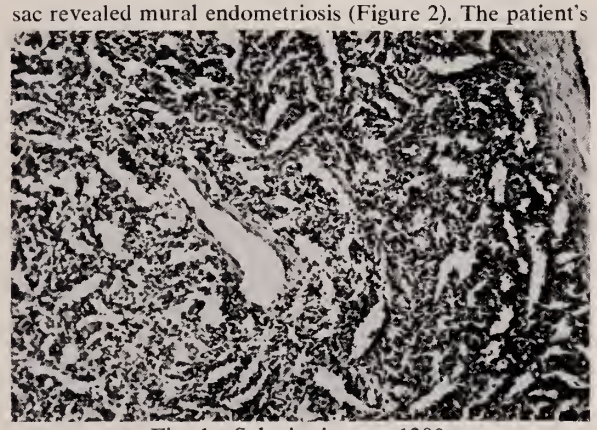


Fig. 1—Splenic tissue x 1300.

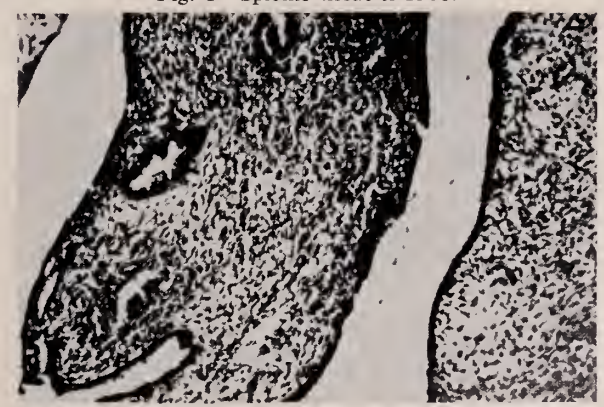


Fig. 2—Endometriosis—glands and stroma x 1300.

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postoperative course was uneventful.

Case 3

A 17-month-old boy was admitted for a right inguinal herniorrhaphy. The inguinal hernia was diagnosed at the age of two months and had not given rise to problems until five weeks before the present admission when it incarcerated. This was treated conservatively because of an intercurrent upper respiratory infection and reduced spontaneously. On re-admission for elective surgery, both external inguinal rings were found widely patent. The testes were in the scrotum. Both inguinal areas were explored and a right inguinal herniorrhaphy was performed. A small yellow nodule suggesting an adrenal rest was noted above the testis on the left and was removed with the hernia sac. The gross impression of adrenal rest was confirmed histologically (Figure 3). The recovery was uneventful.

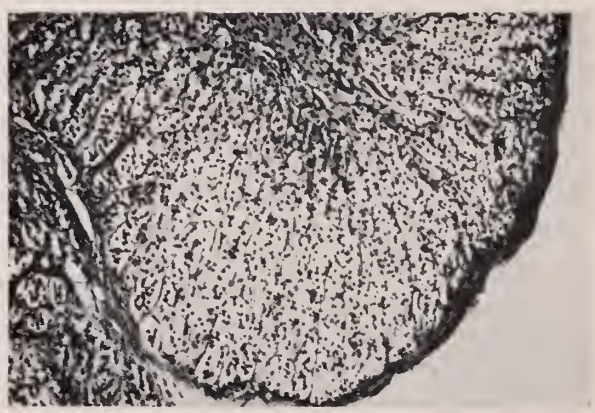


Fig. 3—Adrenal cortical tissue x 1300.

Splenogonadal Fusion

Splenogonadal fusion was first described by Bocstrom in 1883.[15] Watson reviewed the literature in 1968[23] and recorded 52 cases. The anomaly has been described by Sieber[19] as transperitoneal extension of the lower pole of the spleen through a hernial sac and fusion to the normally descended left testicle. There are at least two theories as to embryogenesis. Since the splenic anlage in the dorsal mesogastrium is opposite the genital anlage in the six weeks old embryo, adhesions between the two could account for the subsequent trailing of splenic tissue behind the descending testicle.[20] An alternate theory relates the organ association to the origin of the left spermatic artery from the splenic artery.[13]

The anomaly is either continuous in which case a cord of splenic or fibrous tissue extends from the spleen to the gonad or discontinuous in which case the splenic tissue shows no connection with the main spleen. Of the 52 cases reviewed by Watson,[23] the age range was from birth to 69 years and only four cases were in females; 29 were continuous, 19 discontinuous, and four unclassified. Concomitant birth defects included peromelus and micrognathia. Of the 38 cases diagnosed at operation, 16 had indirect inguinal herniae. All 52 cases occurred on the left side.

This lesion should be distinguished from the accessory spleen, a commonly encountered entity with an incidence ranging from 11 to 35% in various autopsy series.[24] The incidence of accessory spleen is higher when splenic disease is present in youth. The accessory spleen may be found virtually anywhere under the diaphragm and becomes important in splenectomy for a hematological disorder. Accessory splenic tissue may continue to function after splenectomy.

Finally, the lesion should be distinguished from splenosis, a condition in which splenic tissue may be found in abnormal locations (even in the thorax[1]) as a result of trauma[8] or, very rarely, of surgery.[21] Seventy cases have been reported in the world literature.[24] Most have been diagnosed within ten years of traumatic rupture of the spleen although intervals of five months to 32 years have been described. The splenic nodules implanted on peritoneal or visceral surfaces range from a few millimeters to 2-3 cm. in diameter, and there is some evidence of function.[24]

Our case is probably an example of discontinuous splenogonadal fusion because no communicating cord was found. However, such a cord containing splenic tissue might have been overlooked.

Endometriosis

Whereas endometriosis of the umbilicus and of laparotomy scars has been reported frequently, it has rarely been found in a hernia sac.

The first association between inguinal hernia and endometriosis was noted in 1916 by Cullen[3] who reported an adenomyoma of the round ligament fused with incarcerated omentum in an inguinal hernia. In 1926 Sampson[16] reported a case of endometriosis in the sac of a right inguinal hernia associated with pelvic peritoneal endometriosis and an endometrial cyst of the ovary. A further case was reported by Christopher[2] a year later. At the bottom of an oblique right inguinal hernia was a firm fibrous swelling 5 x 4 x 4 cm. which was incorporated into the sac wall. Histologically, this was shown to be endometriosis. Masson in 1945[11] while reviewing 2,686 cases of endometriosis noted two cases with involvement of femoral hernial sacs. Moore in 1957[12] de-

scribed a case in which endometriosis was present in inguinal hernial sacs on both sides, associated with extensive pelvic endometriosis. Serment et al. in 1967[18] reviewed five cases in the literature to which they added another. Two clinical features of interest were cyclic inguinal swelling and pain.

Not all cases of inguinal endometriosis imply hernial sac involvement. Endometriosis may involve lymph nodes in this region.[4] Dormandy in 1956[4] described three cases of extraperitoneal inguinal endometriosis in which, although hernial sacs were present, careful gross and microscopic examination revealed no continuity between the intact peritoneum and the endometriomata. None of the three cases showed involvement of the round ligament. Some cases of inguinal endometriosis, however, are localized to the extraperitoneal portion of the round ligament. Jimenez and Miles in 1960[7] in a review of 16 such cases in the literature pointed out that it was impossible to be sure in some cases whether the lesion represented primary involvement of the round ligament or extension from co-existing hernia sac wall. To these 16 cases, the authors added four further cases of endometriosis of the round ligament presenting as inguinal masses.

Endometriosis presenting in laparotomy scars following pelvic surgery is well known. Its occurrence in a hernial sac is rare and the sequence of events leading to the detection of endometriosis of a post Caesarian ventral hernial sac is distinctly unusual. Gross examination of the specimen would have failed to detect the lesion.

Adrenal Rests

Little has been written on the incidence of adrenal rests in the walls of hernial sacs. In 1919 MacLennan[9] reported small nodules of adrenal rest tissue less than ⅛ inch in diameter in the walls of seven hernial sacs in a series of 700 consecutive herniorrhaphies on children. One of these was lost to study so that the incidence was somewhat less than 1%. All cases were in males, but only 40 of the 700 hernia repairs were in females, making an analysis of sex distribution tenuous. In a subsequent extension of this study in 1922,[10] MacLennan found a total of 18 cases in 1,038 operations on 978 children for hernia. Potter[14] currently describes adrenal rests as occurring quite frequently throughout the peritoneum in infancy, but makes no reference to incidence in hernia sacs.

Although the finding of adrenal rest tissue in a hernial sac wall is of little clinical significance, it lends weight to the contention that all hernial sacs should be examined microscopically in quest of occult pathology.

Summary

Routine microscopic examination yielded three cases with significant pathology in 212 consecutive hernial sacs removed within a 16 month period in a 300 bed general hospital. Two lesions were unsuspected on macroscopic examination. Since subtle lesions may be overlooked both at surgery and on gross inspection, microscopic examination should be carried out on all hernial sacs.

Acknowledgments

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Cervical Disk Disease with Neural Compression

Anterior Surgical Approach

ALBERT L. RHOTON, JR., M.D. AND EDWARD D. HENDERSON, M.D.

SINCE THE PATHOLOGIC process in cervical disk disease originates anteriorly to the cervical roots and spinal cord, it is not surprising that anterior operations have been developed to remove the offending ventral elements directly.[1,2] Nor is it surprising that Mayfield[3] was able to report that the spinal cord and nerve root deficit had not been aggravated in any of 217 patients operated on by the anterior approach: retraction of the spinal cord or nerve root is not necessary to reach the pathologic process by the anterior approach, as it is by the posterior approach. He also noted that after the anterior approach the postoperative course was less painful, because the approach is through soft-tissue fascial planes rather than through posterior neck muscles and because the offending diseased disk is removed and the space realigned and immobilized during the operative procedure.[3] Rosomoff and Rossmann[4] stated that this immobilization prevents further compressive changes in ligaments and apophyseal joints posteriorly and prevents recurrence of disk disease anteriorly. The anterior operation is done with the patient supine, thus avoiding the risk of hypotension and air emboli that exists with the posterior operation, which is done with the patient sitting.

Because of these advantages, five years ago we began doing anterior operations on selected patients who had neural compression from cervical disk disease. Although there are several types of anterior operative approaches, we selected the Cloward technique for patients with neural compression because it gives a better exposure of the spinal canal and the foramen anterior to the nerve roots. The operation is done through a 4- to 5-cm transverse incision made in a skin crease on the anterior neck (Figure 1). The anterior surface of the vertebrae is exposed through the soft-tissue plane between the esophagus and trachea medially, and the carotid sheath laterally. In our 48 cases, there has not been any injury to either of these structures.

After identifying the appropriate disk space with a roentgenogram, the disk is removed (Figure 1). Using a drill ½ inch in diameter, an opening centered at the interspace is extended posteriorly to within a few millimeters of the posterior longitudinal ligament. The last few millimeters of bone in front of the ligament are removed with a small air drill. If the main disorder is a midline ridge or disk, the opening is centered in the middle third of the lateral width of the space, but if the disorder is located laterally, the opening is made off the midline directly in front of the disk deformity.

Can the lateral extent of the intraforaminal portion of the nerve root be decompressed as well by the anterior as by the posterior approach? Raynor and Kingman[5] have shown in cadavers that "the lateral extent afforded by removal of discal material and osteophytes by the anterior approach extends well beyond the point where the root turns ventrolaterally to enter its foramen and is considerably greater than can be accomplished by approaching the nerve posteriorly." After the offending lesion has been removed, a ⅝-inch diameter dowel of iliac bone 1.5 cm long is fitted into the bony opening adjoining the interspace. The bone plug is slightly larger than the bony opening, and this discrepancy restores the interspace height frequently lost with disk degeneration. Cloward[1] has devised an ingenious set of instruments for making the bony opening and obtaining the bone graft from the iliac crest; they ensure that the bone plug fits snugly into the bony

From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

See editorial, page 1014.

opening so that the space is immobilized once it is in place.

Results

In the last five years we have performed anterior operations on 48 patients for cervical root or cord compression. The anterior operation was the first or primary operation done to relieve the neural syndrome in 40 patients, and was done on another eight patients after a posterior operation had failed to give the desired relief. Patients ranged in age from 33 to 75 years. One patient was below 40 and one above 70. The numbers in the fifth, sixth, and seventh decades were 17, 20, and nine, respectively.

The results were much better in the group on which the anterior procedure was primary, and this group will be reviewed first. Of the 40 operations, 34 were for root compression and six for cord compression. Seventeen of the root lesions were caused by soft disk herniations and 17 by foraminal osteophytes alone or associated with soft disk protrusions. One patient had a C-5 and one a C-8 root lesion; the remainder of the root lesions were nearly equally divided between the C-6 and the C-7 roots. All patients who had root lesions were free of pain at the time of dismissal from the hospital and only one patient is known to have had a recurrence of pain later; this gradually subsided after the patient wore a cervical collar for a brief period. To ensure that the fusion

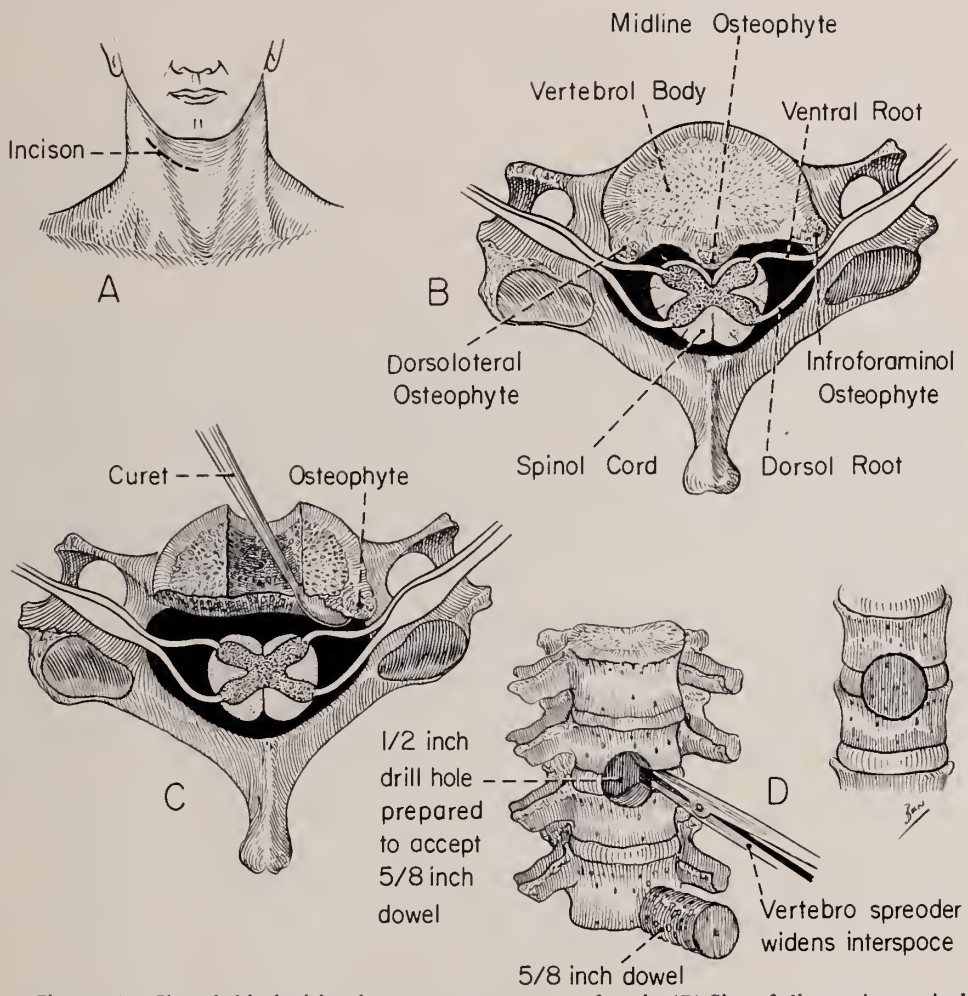


Fig. 1—*(A)* Site of skin incision in a transverse crease of neck. *(B)* Site of disease in cervical spondylosis. This cross section of cord and spine at midcervical region shows intraforaminal, dorsolateral, and midline osteophytes. *(C)* Same cross section as in *B*, showing bony opening into spinal canal which adjoins disk space; crosshatches show area of bone that can be removed to decompress cord and nerve roots. *(D)* Anterior view of spine showing the half-inch diameter opening in vertebra adjoining the disk space. *(E)* Bone plug fitted into opening; since plug is ⅝ inch in diameter and bone opening is half inch, when it is inserted interspace height is restored.

was solid, all patients had lateral and anteroposterior roentgenograms. in flexion and extension, six to eight weeks after surgery. The six patients who had cord compression (Figure 2) preoperatively did not have any increased deficit after surgery; four patients improved and two did not. Regardless of whether an anterior or posterior operation is to be done, all patients who have cord compression are told, preoperatively, they should be satisfied with the results of surgery if it prevents a further progression of their neurologic deficit.

Forty-one of the 48 patients had only one space fused (Figure 3); two spaces were fused in five patients and three in two patients. Fusion was done only at the level of neural compression and multilevel fusions were done only because there was evidence of neural compression at several levels on neurologic examination or on the myelogram.

The results have been less satisfactory in the eight patients who were operated on by the anterior approach after failure of a posterior operation at this institution or elsewhere. Although the deficit was not aggravated by the anterior operation in any of these patients, only three of seven who had cervical radiculopathy obtained satisfactory pain relief and the one patient with cord compression did not improve. Most of these patients had foraminal osteophytes, and after the posterior operation they were left with a constant ache and dysesthesia in the arm that was usually associated with a persistent root deficit. One patient in this group was found subsequently to have a neurofibrosarcoma of the brachial plexus; as expected, this operation failed to relieve the pain.

There were no permanent complications in this group of 48 patients nor was the neurologic deficit increased after surgery in any patient. Two had transient unilateral vocal cord paresis which had disappeared six weeks after surgery. The only other complications were saphenous phlebitis in one patient and infection at the iliac-crest donor site in another.

Discussion

Seventeen posterior-approach operations for cervical disk disease were also done by one author (A.L.R.) while this series of 48 anterior operations was in progress, and consequently patients having both types of operation were on the neuro-

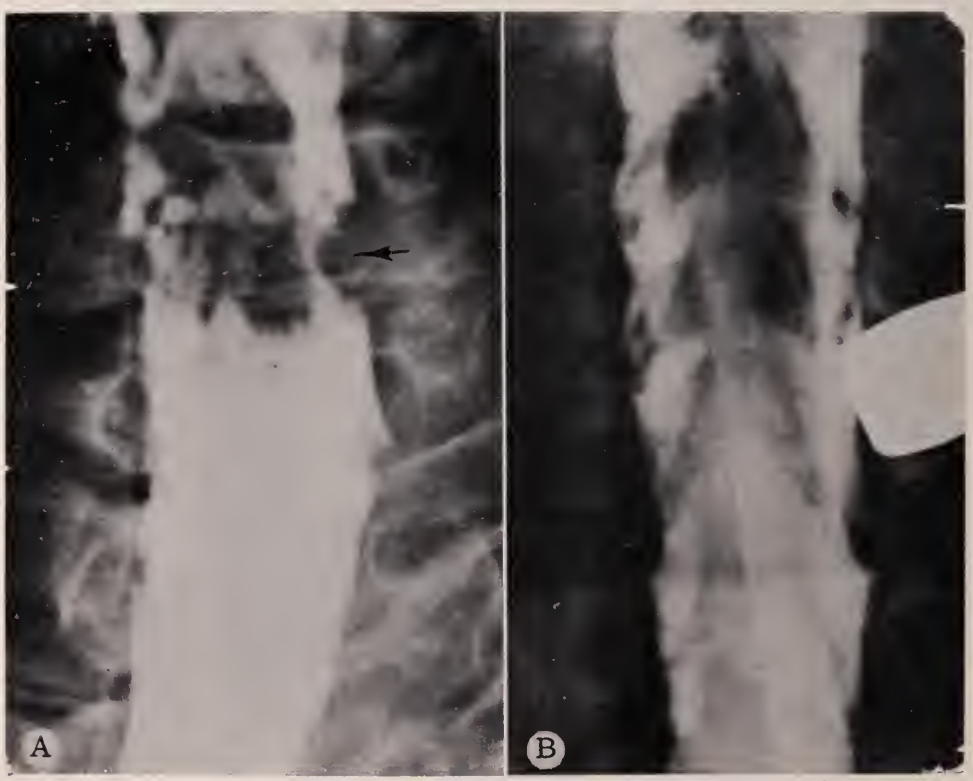


Fig. 2—*(A)* Anteroposterior view of Pantopaque myelogram of cervical spine in patient with spinal cord compression showing partial block *(arrow)* at C-6. *(B)* Same view of myelogram done three years after anterior removal of ridges and fusion, showing normal flow of Pantopaque and absence of ridges.

surgical service at the same time. Observing the postoperative course of these two groups has led us to conclude with Mayfield[3] that the anterior approach offers a less painful postoperative course than the posterior approach. There are two reasons for the lesser amount of pain postoperatively with the anterior approach. Firstly, the anterior approach through the soft fascial plains of the anterior neck causes less pain than the posterior approach through the muscle and fascial attachments to the spinous processes and lamina. Secondly, the offending disk space is immobilized by the tightly fitting bone graft after the anterior but not after the posterior approach. Interestingly, five of the patients in this series were physicians who came to the Mayo Clinic requesting the anterior operation for their cervical radiculopathy because they had arrived at similar conclusions after observing results in their own patients who had had both types of operation.

Although the anterior approach avoids some of the complications of the posterior approach in the sitting position, such as anesthetic and positioning problems, air emboli, and cerebral symptoms from hypotension, it does expose the patient to a different set of potential complications.[6] The most frequent is transient recurrent laryngeal palsy, which occurred in two of our patients. Other rare complications, not seen in this series, are esophageal and vertebral artery injury or Horner's syndrome due to injury of the cervical sympathetics.

The type of fusion done with the anterior operation does introduce the risk of pseudarthrosis and development of a "swan neck" deformity, but this did not develop in any of the 53 spaces fused in this group of patients. In fact, our series includes two patients on whom anterior operations were done because of cervical spine deformities with neural compression that followed posterior laminectomy. Critics of the anterior approach have cautioned correctly that a fusion does increase the strain on the adjacent disk spaces, which are rendered more susceptible to degenerative change. This effect has not occurred in this series, but the longest period of follow-up is only five years. Although anterior-approach operations have been done for over 10 years elsewhere, with some series registering over 500 cases, there are no data to indicate that postoperative deformities are going to be greater after the anterior than the posterior approach.[3,7]

Early in this series we were doing anterior operations only on patients who had foraminal osteophytes with neural compression because the results after posterior operations on foraminal



Fig. 3—*(left)* Lateral view of cervical spine showing severe degenerative changes at C-5 and C-6 interspace. Patient had neurologic evidence of root compressed only at C-6 space. *(middle)* Anteroposterior view of Pantopaque myelogram of cervical spine showing myelographic defect at C-6 space on right side *(arrow)*. *(right)* Lateral view of cervical spine taken after anterior decompression and fusion at C-6 space which was the level of neural compression; bone plug is in place at C-6 space *(arrow)* and interspace height has been restored. The C-5 space was not fused because there was no evidence of neural compression there.

osteophytes were less satisfactory than those for soft disk herniations. When it became obvious that patients with foraminal osteophytes operated on anteriorly had less pain postoperatively than did patients with soft disks operated on posteriorly, and that the anterior exposure was adequate to deal with soft disk herniations, we began operating on the soft ruptured disk, with similar good results. Although patients having the anterior operation for soft disk removal have less neck pain during the first month after surgery than do patients having the posterior approach, there seems to be little difference in the amount of pain thereafter.

If the cervical cord is compressed by spondylitic ridges at only one or two levels, an anterior operation is done; however, most of our operations for spinal cord compression are done posteriorly because the ridges causing cord compression are frequently present at more than two spaces. We are concerned that multi-space fusions will be associated with an unacceptably high incidence of deformity at adjacent spaces, although there is as yet no data to support this concern, and Rosomoff and Rossmann[4] have reported good results in patients who had cervical myelopathy with multiple level fusions.

On the basis of this series of 44 patients operated on at 53 spaces, we conclude that when the preoperative diagnosis is definite, the anterior approach is adequate to deal with the radiculopathy associated with foraminal spurs and ruptured intervertebral disks, and with the myelopathy due to cord compression at one or two levels.

Summary

The results of anterior cervical diskectomy with interbody fusion done by the Cloward technique are reviewed. On the basis of this series of 48 patients we conclude that the anterior approach is adequate to deal with the radiculopathy associated with foraminal osteophytes and ruptured intervertebral disks and with the myelopathy due to cord compression at one or two levels. The results were much better in the group of 36 patients on whom the anterior operation was the first or primary operation than it was in the group of eight patients on whom it was done after a posterior laminectomy had failed to control the symptoms. The neurologic deficit was not increased after surgery in any patient. The most common postoperative complication was a transient recurrent laryngeal palsy in two patients.

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Distinguished Physician

Dr. Leslie Zieve, associate chief of staff for research at the Veterans Administration Hospital in Minneapolis, has been appointed a "distinguished physician," one of the highest honors of the Veteran's department of medicine and surgery.

Dr. Zieve has been a professor of medicine at the University of Minnesota since 1962 and is a member of the graduate school faculties in both medicine and biochemistry.

He is the eighth physician in the Veterans Administration to be honored by the appointment. Those appointed to the rank of "distinguished physician" are expected to enhance the various activities "essential to the achievement and maintenance of the highest quality of clinical care in the hospitals of the Veterans Administration."

Dr. Zieve has made major contributions in the field of research, especially in the study of liver function tests and liver disease.

Actinomycosis of the Female Genital Organs

GERHARD O. RICHTER, M.D., JOSEPH H. PRATT, M.D., DONALD R. NICHOLS, M.D. AND CAROLYN B. COULAM, M.D.

A LETTER FROM a woman who had had actinomycosis of her genital organs and who subsequently has been delivered of several children prompted us to review the cases of the Mayo Clinic since the reports of Paalman and associates.[1] In the literature on actinomycosis of the female genital tract, five major review articles exist: by Bucura[2] with 67 cases, to which Hartl[3] added 88 cases; by Cornell[4] with 72 cases, to which Paalman and associates[1] added 45; and by Daniel and Mavrodin[5] with 66 cases. Since 1951 reports of cases have been published by many authors.[6-22] Cross-checking the five major reviews and adding the 17 cases published since, we gathered a total of 196 cases. Not available and, therefore, not included in this summary are reviews in the Russian literature by Karasew[23] with 99 cases, to which Karabanov[24] added another 28, and the cases by Traub and Kovacs,[22] Batizfalvy,[25] Trebicka-Kwiatkowska,[26] Gridaladze and Tataradze,[27] Zawirska,[28] and Podar and Meipalu[29] published in Russian, Polish, and Hungarian journals. Including the two cases (reported herein) that were seen at the Mayo Clinic after Paalman and colleagues[1] had given their report, there are 199 cases published in the western literature until 1964 and more than 300 in the world literature.

This report describes two cases, which illustrate the existing long course of the disease with the possibility of relapses, the excellent outcome after treatment with penicillin, and, in one case, the occurrence of several pregnancies after the actinomycosis was cured.

Report of Cases

Case 1

A 16-year-old white girl was seen for the first time at the Mayo Clinic on Mar. 23, 1947. She had been well prior to an appendectomy performed at another institution in August 1945 (when she was 14 years old) because of generalized abdominal pain; the abdominal pain increased after the operation. Because of the persistence and increased severity of the pain, combined with continuing amenorrhea, dilatation and curettage was done on two occasions several months apart, resulting in temporary relief. One month after the second dilatation and curettage, a "urinary bladder infection" developed and the patient passed a blood clot in the urine. She was then referred to the Mayo Clinic.

She had lost 20 lbs. during the two month prior to referral and was acutely ill during the five days just prior to her examination, with severe abdominal pains, anorexia, chills, and a temperature as high as 102 F. For two days she passed gas but no stool.

On physical examination, she had a pulse rate of 116 beats/min and was acutely ill and anemic. The abdomen was distended, very tense, and tender, especially in the lower quadrants (on the right side more than on the left). There was no visible peristalsis. The uterus was small, fixed by a firm, hard, indurated, 5- by 6-cm mass on the right that extended into the cul-de-sac. Rectal examination revealed exquisite tenderness anteriorly.

The hemoglobin value was 9.4 gm/100 ml; erythrocyte count 3,060,000 cells/cu mm; leukocyte count 19,900 cells/cu mm; and sedimentation rate 80 mm in one hr (Westergren). Urinalysis showed albuminuria of grade 2 and pyuria of grade 3. The chest roentgenographic findings did not show any abnormalities, but a simple roentgenogram of the abdomen revealed many dilated loops but no air-fluid levels. A presumptive diagnosis of tubo-ovarian abscess or pelvic neoplasm was made, and treatment was given with fluids intravenously, a Miller-Abbott tube, sulfadiazine, penicillin, and streptomycin.

In April 1947, an abdominal exploration revealed two pelvic abscess cavities, one behind the bladder and one in the right pelvis. Each abscess contained greenish yellow, nonodorous pus and was drained without excision of any of the pelvic organs.

The bacteriologic cultures grew *Actinomyces bovis*. After surgery, the patient received, by eight intramuscular injections per day, a total of 20,500,000 units of penicillin in 18 days, and 9.5 gm of sulfadiazine orally. The patient was dismissed from the hospital on the 22nd postoperative day. One month later she received another course of 12,000,000 units of penicillin.

The patient was asymptomatic until June 1950, when an examination at another institution revealed a cystic mass in the left adnexal region. The mass was considered

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a postinflammatory ovarian cyst.

In September 1950, the patient again had severe lower abdominal pain. The pain increased when the bladder was full and was relieved by voiding. No fever, chills, or vaginal discharge was noted. The patient had lost 15 lbs. within three months.

Physical examination revealed the uterus fixed by a large cystic and hard, irregular, nodular mass filling the cul-de-sac and constricting the rectum. The mass extended posteriorly to the right wall of the pelvis. The adnexa were not identifiable. In October 1950, an incision was made and drainage was performed through a posterior colpotomy. An abscessed cavity could not be found in the indurated mass, and cultures did not grow *A. bovis*. This time, 25,500,000 units of penicillin were given during a 24-day period. In November 1950, the patient was dismissed. She received 1,200,000 units of penicillin daily for another month.

Except for fecundity, the patient has had no pelvic problems since 1950. The patient became pregnant and delivered her first child in 1952. Subsequently she has had five other full-term pregnancies.

Case 2

A 30-year-old woman, gravida 3, para 3, with a normal menstrual history, was first seen at the Mayo Clinic on April 23, 1946. She was referred for possible surgical treatment of a "rectal tumor." She had had no bowel or rectal symptoms until two months before her admission to our clinic, when she noted the onset of progressive difficulty in moving her bowels, with the feeling of incomplete evacuation. She denied any history of blood or mucus in the stool. Six weeks before, the patient had been examined by her family physician, who found an indurated rectal mass and referred her to a local surgeon. A colostomy was performed for obstruction of the bowel in the left lower quadrant. At surgery, the mass was seen infiltrating around the rectum and into the broad ligament. A biopsy specimen was not taken. A node was taken and showed inflammatory tissue. After the operation, the patient did well and was referred to our clinic for consideration of further surgical treatment. For three to four days before her arrival, she noted stool in the rectum as well as in the colonic stoma. She had lost 23 lbs. since the onset of her trouble.

On physical examination, her temperature was 99.5 F, but her pulse rate and blood pressure were normal. She was obese but in no acute distress. The positive physical findings were restricted to the abdomen and pelvis. The liver and spleen were not palpable. There was a small, single-barrel colonic stoma, but no masses were felt. The uterus was large, with some thickening in the left adnexal area. The lumen of the rectum was narrowed but regular, with soft-tissue thickening on the left. Proctoscopy and biopsy revealed inflammatory mucosa. The Frei test was negative. The hemoglobin value was 10.6 gm/100 ml, the leukocyte count was 9,600 cells/cu mm, and the sedimentation rate (Westergren) was 99 mm in one hour. A roentgenogram of the chest showed no abnormality.

The patient returned home for six weeks to take warm soda enemas and hot sitz baths three times each day. She was advised to return for closure of her colonic stoma. She returned on June 10, 1946, feeling wel Her stools had been of normal caliber and color an nearly all from the rectum. On physical examination her temperature was 99 F. The size of the coloni stoma was decreasing, and the pelvic and rectal finding were the same as in the previous examinations. Procto scopy revealed a persistent inflammatory process in th rectosigmoid region. Examination of the stool for para sites and ova was negative. In the hope of hurryin resolution of the inflammatory process, the patient re ceived two courses of deep x-ray treatments on two consecutive days; each dose delivered 130 kv to the pelvis She returned home to continue therapy with enemas and was to return in six months for closure of her colonic stoma.

On Dec. 10, 1946, she returned to our clinic. She had had no digestive disturbances for the past six months. The stoma had become smaller, with little stool passing through it. Her temperature was 98.6 F. Pelvic examination revealed a firm mass extending upward from the uterus to the left and fixed between the uterus and sigmoid. Exploratory laparotomy in December 1946, demonstrated a left tubo-ovarian abscess. A left salpingo-oophorectomy was carried out, preserving the right tube and ovary. The colonic stoma was closed at the same time. Pathologic examination of the surgical specimen revealed multiple granulomatous actinomycotic abscesses involving the left tube and ovary. After the operation, the patient did well. She was given penicillin intramuscularly and was dismissed in December 1946.

The patient returned to our clinic on March 3, 1947. She had been doing well until seven to 10 days prior to her arrival, when she noted urgency and frequency of urination. Her family physician gave her medicine to relieve her urinary complaints. However he could not feel a mass in her pelvis. The patient had had normal bowel movements since closure of the colonic stoma. The uterus was partially fixed on the right side with a palpable, fixed, right adnexal mass. The infection from the *Actinomyces* seemed to have extended, and the patient was treated with penicillin and sulfa for four days before subtotal abdominal hysterectomy, right salpingo-oophorectomy, and appendectomy were performed. A right tubo-ovarian abscess had perforated onto the brim of the pelvis and had incorporated the appendix. Cultures from the right ovary subsequently grew *A. bovis*. The patient's postoperative course was uneventful. She received penicillin and sulfa and was discharged on the 16th postoperative day.

The patient was not seen or heard from again until she answered a letter inquiring about her well-being in 1965. In her letter she stated that she has had no further medical or surgical treatment and has been enjoying good health.

Comment

Six patients (four of whom formerly had been reported by Paalman and associates)[1] had long-term follow-up. Of the six patients, one died from active actinomycosis; the cause of death presumably was glomerulonephritis. No permission

or autopsy was granted. All five surviving patients responded to follow-up letters in 1965, and all stated that actinomycosis had not recurred and that their health was good. One patient had recurrence of the pelvic infection after three years in which she was asymptomatic, but ultimately she was cured. This same patient later became the mother of six children. After being treated for pelvic actinomycosis one patient underwent repair of an incisional hernia and a second underwent cholecystectomy; the abdominal cavity of each patient was free of adhesions. Pelvic examination with the aid of anesthesia revealed minimal adhesions in a third patient.

Actinomycosis of the female genital organs is a rare disease. About 60% of all patients with actinomycosis have the infection in the cervicofacial region, 20% in the thorax, and 20% in the abdominal region. Even among the group with abdominal involvement, genital actinomycosis is rare. Putnam and associates[30] found that among 122 patients with abdominal actinomycosis at the Mayo Clinic only 10 had actinomycosis of the genital tract. Since the advent of penicillin, the disease seems to be even rarer because *A. bovis* and *A. israeli* are sensitive to antibiotics. Such treatment, in many cases, prevents actinomycosis after appendectomy or perforation of the large bowel or makes it relatively easy to cure a patient with advanced actinomycosis. Whether there is an actual decrease in the incidence of actinomycosis is not known but, interestingly, only 25 cases of pelvic actinomycosis were found in the literature in the 15-year period from 1950 through 1964 (Table), when treatment of actinomycosis with an antibiotic was routine, whereas in the 15-year period from 1925 through 1939, 87 case reports were found.

An exogenous entry of *Actinomyces* by the chewing of grasses or grains was postulated formerly, but this theory has been disproved because *Actinomyces* organisms are found in the gastrointestinal tract of only a few animals, including man.[1] MacCarthy[17] attributed 91% of 157 cases to an infected appendix.

Putnam and associates[30] noted that 103 of 122 patients with abdominal actinomycosis had had emergency surgical procedures for perforations of the gastrointestinal tract before the development of this disease, but in genital actinomycosis, this relationship is much lower. The symptoms differ from patient to patient.

Our patient (Case 1) was especially interesting since she is the only one in the available literature who not only has become pregnant but has delivered living children. All pregnancies progressed normally and were delivered vaginally.

TABLE

Previously Reported Cases of Actinomycosis of the Female Genital Organs

Year	Number of cases
Before 1890	4
1890-1904	20
1905-1919	26
1920-1934	51
1935-1949	71*
1950-1964	25
Total	197

*Includes 10 cases seen at the Mayo Clinic up to report of Putnam and associates.[30]

Treatment

In many cases, an abdominal exploration is necessary for diagnostic purposes. Surgery consists mainly of incision and drainage of abscess pockets, after which microscopic and bacteriologic examination of pus and tissue is done.[31] If these examinations are suggestive of actinomycosis, removal of the mass and total abdominal hysterectomy or either unilateral or bilateral salpingo-oophorectomy may be performed for the older patient. In younger patients, however, the treatment should be conservative, consisting only of draining the abscesses. The results of treatment with antibiotics are excellent, and there is so little formation of adhesions that pregnancy is possible.

All strains of *A. israeli* or *A. bovis* are sensitive to penicillin and tetracycline in vitro, and most strains are sensitive to streptomycin. All strains of the fungus that we have cultured have been inhibited by 0.1 μg or less of penicillin G per cubic milliliter of culture medium. Our experience[32] in treating more than 150 patients who have had actinomycosis involving various portions of the body has established that both penicillin and tetracycline are effective agents. If the disease has been present sufficiently long to permit an overgrowth of fibrous tissue, formation of sinuses, or an impairment of the general health, effective management of the infection has been much more difficult and chemotherapy over many months has been necessary.

In actinomycosis, if penicillin is selected for the treatment, at least 1,000,000 units of procaine penicillin G should be given intramuscularly daily for a minimum of six weeks. Penicillin G or V

orally can be tried when the infection is mild, but the intramuscular route of administration is preferable for the more extensive forms of the disease.

Various studies and our own experience have indicated that the tetracyclines also are effective agents in the treatment of actinomycosis. The usual program that we have followed in recent years has been the use of tetracycline, 500 mg every six hours orally, for at least four weeks. We have found it necessary at times to administer the tetracycline for six months or more before we have had evidence that the fungus has been eradicated. Although penicillin has been regarded as the drug of choice in the treatment of actinomycosis, tetracycline in some instances may be preferable, particularly in patients who are allergic to penicillin.

In certain patients in whom response to a single antibiotic has been disappointing, we have used streptomycin in addition to penicillin or tetracycline. Results with this combined therapy have been sufficiently encouraging to warrant further investigation of such a program. If streptomycin is used, the daily intramuscular dose should not exceed 1 gm, and the drug should not be used longer than four weeks at this dosage.

The results of treatment with antibiotics are excellent. Whereas actinomycosis was formerly almost always fatal, the susceptibility of *A. bovis* or *A. israeli* to antibiotics has changed this during the past 25 years. Every case report formerly stressed the long protracted course and the small chances of cure; however, all reports since 1950 agree on the good results with antibiotic treatment. Of 17 patients whose case reports were available to us, only one patient with genital actinomycosis died; both diagnosis and treatment were delayed. Of the six patients seen at the Mayo Clinic since 1945, only one died, while suffering from an active actinomycosis, presumably from glomerulonephritis. The other five patients were alive and well, 12 to 19 years later.

Summary

Two cases of actinomycosis involving the female genital organs are added to the existing 197 reports in the literature. Both patients were cured by combining surgery with antibiotic therapy. The number of reported cases of actinomycosis involving the female genital organs has decreased greatly during the past 20 or 25 years, probably because of treatment with antibiotics. The clinical course has been shortened markedly, and the chance of survival of the victim with this once fatal disease is nearly 100%. Surgical treatment in young girls should be conservative. One of our patients treated by drainage of abscesses and with penicillin was subsequently able to bear six children.

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Editorials

The Accident Prone Physician Pilot

Is flying a suitable avocation for physicians? The question arises after reading an account of 15 fatal accidents involving physician pilots.* All of these accidents were chargeable to pilot error. None was caused by engine failure. Three airplanes had "structural" failure (read: the airplane fell apart in the air) in every case due to pilot error imposing excessive stress on the airframe. Nine involved flight into weather conditions beyond the ability of the pilot to handle. Eight involved night flying. One of these pilots took off for a flight northwest; was observed by the tower operator to be flying southeast and changed course only after his reciprocal bearing was pointed out. A pilot took off with his controls locked. One inadvertently landed downwind. Two were drunk. (Numbers are greater than 15, because in several there were multiple factors involved). It is evident from these reports that some of these pilots scarcely knew which end of an airplane was up when they took off with their passengers on their last flight. The article does not state the base, the total number of physicians currently flying, but a ballpark figure for the United States is 3600 based upon the 2400 membership of the Flying Physicians' Association and the estimate that two out of three physician-pilots belong.

So the annual fatality rate for 1971 is 420/100,000, right up there with heart disease, cancer and stroke. Actually a total of 42 people were killed in these 15 accidents, but there is no base figure for passengers.

One pilot attempted a night landing at his home base of Atlantic City but unfortunately confused east for west and with a west wind gusting up to 23 knots landed toward and eventually into the Atlantic ocean. Four drowned. Can anyone conceive the egregious error of a takeoff with the controls locked? A physician managed to do that. One of these fatal 15 in 200 hours of flying never bothered to increase his student rating.

If one common failure can be pinpointed among these sorry stories it is the lack of respect shown by these flyers for their machine and the art, coupled probably with unwarranted over evaluation of their own flying skill. It may be that long indulgence in careless practice of medicine with errors suppressed and mitigated by a forgiving nature leads to a similar approach to flying where errors are more sternly punished.† Safe flying is a personal matter, an over-riding desire to do it right. Flying instructors, Federal Aviation Authority examiners can assist but fundamentally safety is self-engineered.

Surely physicians can fly, thousands fly well and safely. But there are hazards, 99% of which are generated within the man (in this particular group, 100%). Physicians who fly or plan to take flying training are urged to read the article in the July 1972 issue of The Flying Physician. It will be a heuristic experience.

Reuben Berman, M.D.
Samuel I. Berman, M.D.
Minneapolis, Minnesota

*Woods, P: Fatal M.D. Pilot-in-command flight accidents. The Flying Physician 15:28. 1972.

†The flight instructor has difficulty establishing a teacher-student relationship with such a doctor. He may never be able to instill proper aviation discipline.

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4. Multiple brokerosis.

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Hysterical Neurosis

Doctor Flemenbaum* sharpens the clinical description of the hysterical neuroses. He directs attention to certain of these patients whose elaborate neurotic defenses make accurate diagnosis difficult. Actually, because of the more refined diagnostic methods for physical disease and because of increased psychiatric knowledge among all physicians, the number of patients suspected of having conversion disorders is increasing. It is no longer sufficient to recognize only the patient who is obviously mimicking organic disease; the seductive, dramatic, paralyzed young woman, indifferent to her plight, is more a caricature out of psychiatric annals than a real representative of the somatisizing neuroses.

Flemenbaum emphasizes that an increasing proportion of hysterical patients give a premorbid history not of obvious superficiality, helplessness, and inadequacy but rather of competency and self-sufficiency (albeit superficial or inconsistent on more careful examination). Rather than the patient being suddenly incapacitated, the course is one of having gradually to "give in" to long-complained-of illness and give up "cherished" responsibilities. Highly symbolic stresses less commonly contribute to the conversion than a family or physician that reinforces the "illness."

As diagnostic sophistication increases, and as we begin looking at the male more objectively, I suspect that the apparently high ratio of women to men with conversion hysteria will diminish. This is already obvious in the area of the compensation neuroses.

David W. Swanson, M.D.
Rochester, Minnesota

*Flemenbaum, Abraham: Hysterical neurosis. Minnesota Med 55:9:853, 1972.

Left Ureteral Obstruction

The recent report by Gilman, et al.* of left ureteral obstruction following ileac diversion of urine adds another cause to the growing list of late complications to this procedure. Gilman documents five cases out of eighty seven ileac diversions in which three cases revealed obstruction of the left ureter as it hooked under the inferior mesenteric artery. As Gilman stated, bringing the ureter through the mesocolon anteriorly would probably eliminate the problem. Other major complications such as obstruction at the skin and anastomatic levels, stasis, reflux, infection and stone formation have been reported as high as twenty five percent in some series of cases following ileac diversion. The benefits of the operation are great in patients who must have this form of diversion but the risks are significant. Candidates must be carefully evaluated. Ileac diversion should be reserved for malignant disease, neurogenic disease of permanent nature and only certain other irreversible conditions.

Gordon W. Strom, M.D.
Minneapolis, Minnesota

*Gilman LS et al.: Left ureteral obstruction. Minnesota Med 55:9:784, 1972.

Pancreatic Scanning

Doctor McGill, Wahner and Tauxe* present an interesting comparison of observer variation in accuracy of pancreatic scan interpretations alone. One important cause of these variations appears to be differences in confidence or at least in willingness to avoid the "indeterminate" category. If we all could more easily identify and learn to accept an "indeterminate" scan as just that, we could at least hope to reduce the number of false positives and perhaps obtain better service from this technique in an area in which other non-surgical methods have had great limitations.

Stanley C. Von Drashek, M.D.
Minneapolis, Minnesota

*McGill DB et al: Pancreatic scanning. Minnesota Med 55:9:796, 1972.

Cervical Disk Disease with Neural Compression

THE ARTICLE by Doctors Rhoton and Henderson* from the Mayo Clinic appearing in this issue of MINNESOTA MEDICINE is both informative and timely.

It has long been recognized by neurosurgeons that the classical posterior cervical approach for bony osteophytic spurs or so-called "hard discs" often times leads to less than optimum postoperative results. Because of the anatomy involved, it is frequently very difficult or impossible to satisfactorily remove the hard, bony osteophytic spur lying immediately anterior to the nerve root. In such situations, it is not unusual to have patients return with persistent complaints of pain, sensory disturbances and continuing motor dysfunction.

The anterior approach, as outlined in this article, makes it possible to remove the offending osteophytic spur or spondylotic ridge quite completely. It has been our practice to carry the dissection to the posterior longitudinal ligament, then incise the ligament and using a small, 45-degree angled Kerrison rongeur, remove the ligament and the spondylotic ridge or spur by working in the plane between the ligament and the anterior aspect of the dura mater. We feel that a thorough removal of the osteophytic spur can thus be effected.

Our experience with this type of operation reveals that the best results occur when only one interspace is involved. We have done a good number of two level fusions, but the long term followup has not been as rewarding as with the single lev We have seen a number of patients who have h three to five level fusions done elsewhere wl persist with a multitude of complaints referable the head, neck and arms.

Consequently, if the disease process of the ce vical spine is not limited to one or two levels, v feel that the posterior approach with a wide d compressive laminectomy, foraminotomy and de tate ligament section, should be carried out.

Our experience with one or two level fusio for osteophytic spurring and spondylotic ridges excellent and corroborates the authors' result We have little experience with the anterior a proach for acutely ruptured intervertebral disc It has been our practice to deal with these fro the posterior approach. With the excellent resul reported in this article, perhaps more ruptur cervical discs should be dealt with anteriorly.

This procedure is not only useful in handlir spondylotic ridging, osteophytic spurring and ru tured cervical discs, but also in select cases, has been helpful in dealing with fractures of th cervical spine.

The anterior surgical approach to certain di ease processes of the cervical spine has withstoo the test of time and has proved to be a highly su cessful procedure in the neurosurgeon's operativ armamentarium.

Erich S. Wisiol, M.I
Minneapolis, Minneso

*See page 998.

Longstanding Colon Polyp Malignancy

CARCINOMA OF THE colon continues to be an important medical entity. It is currently estimated that approximately 12% of all cancers arise from the colon or rectum. An estimated 47,000 deaths directly attributable to colon cancer are expected in 1972. What is further discouraging is that the death rate from colon cancer has not changed significantly in the past 30 years. Routine medical evaluation, proctoscopic examinations, stool analysis and periodic roentgenographic bowel evaluations have not enhanced significantly the early detection of colon cancer. Surgical procedures and medical treatment have not altered survival significantly.

In a case report in this issue, Mongé* discusses the relevance of a colonic polyp as it relates in time to the development of a carcinoma.

Medical literature is controversial regarding the premalignancy of colon polyps; yet there does seem to be some poorly defined relationship between certain adenomatous polyps and carcinomatous changes.[2-5] Clearly, what is needed is a tumor specific test that would detect early colonic cancer.

See page 986.

Gold[6] in 1965 reported the discovery of an antigen found in high proportions (97%) in patients with colon cancer. As yet this test is not readily available to most physicians. Further investigation of this carcinoembryonic antigen (CEA) has shown this not to be specific for colon cancer.[7] The CEA assay currently appears to be useful in the followup of patients with colonic cancer, and in the future, may be more of a diagnostic aid.

Barium examination of the colon may reveal early mucosal changes as well as polyps, but the histologic diagnosis remains essential. The clinical decision to obtain tissue by laparotomy is many times difficult. Recent wide spread use of the fiberoptic colonoscope has enabled physicians to view the entire colon, biopsy suspicious lesions, and snare pedunculated polyps.[8-9] This instrument makes histologic diagnosis much easier and serves as a way of following mucosal alterations.

Utilization of all the available techniques will bring about a better understanding of which polyps are most likely to undergo malignant changes, and in effect help make the diagnosis of colonic cancer earlier.

Neil Hoffman, M.D.
Minneapolis, Minnesota

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Technique for Placing Umbilical Catheters

This article by Dr. Strickland* poses one of the philosophic questions for which there is no glib answer. The use of a catheter in the umbilical vein has made exchange transfusion possible and relatively safe in almost any general hospital with a good laboratory and a obstetrical department. The use of arterial and venous catheters to monitor blood gases in critically ill infants poses the relation of risk to salvage. It is not possible to monitor all ill newborns in every community hospital, nor can every pediatrician become as adequate a neonatologist as Dr. Strickland. It seems we should lean more and more to centers where the high risk infant can be cared for. Often times, the risk of travel to a center is less than the risk of hazardous procedures in unskilled hands.

S. L. Arey, M.D.
Minneapolis, Minnesota

*See page 1021.

Cover Photograph

"November Song"

The photograph on the cover of this month's issue was taken by Dr. John Wendland five years ago during a trip he and his family made to enjoy the fall foliage. He recalls the area as being around Red Wing and at the time was impressed with this particular field of wheat as this method of harvesting wheat is disappearing from the farm scene. Most of this is done by combine.

Dr. Wendland is an ophthalmologist practicing in Minneapolis, a clinical professor of Ophthalmology at the University of Minnesota and a consultant in ophthalmology at the Veterans Hospital. He skis, climbs mountains and excels in making motion pictures for his personal use.

Letter to the Editor

To the Editor:

The latter-day barber surgeon, dignified as the "assistant physician,* "the medico." "serving a doctorless town," may be defined as an ex-corpsman or a former hospital orderly or other attendant who has taken a two-year course in the intricacies of assisting a physician. (To become a licensed physician without specialty requires nine years.)

After nine months of didactic training in courses of anatomy, physiology, physical diagnosis, and electrocardiography, the "assistant physician" may spend 15 months more in clinical experience, rotating through a four to eight weeks' course in the practical aspects of the various specialties of medicine and surgery. (To become a specialist in medicine or surgery requires three to six more years.)

In this "clinical arena" he learns "how to attend the patient's needs, order appropriate laboratory tests, make rounds, and assume other responsibility."

This novitiate in medicine is proudly endorsed by health care organizations and by politicians as a panacea for the delivery of health care; for what more ideal method of wooing the voter into Federally-controlled medicine is there, than supporting a solution for an erroneously developed public-image: the medical-care impasse!

The medico has found that his greatest contribution was by having "him work at the hospital while his physician spends most of his time in the office."

The assistant physician feels that he is competent to do a complete history and to make a complete physical examination, "including pelvic examinations on women;" he also maintains that he can arrive at a tentative diagnosis and order the appropriate laboratory tests. And, believe it or not, he feels that his service is not even used to its full potential, because he believes that he can be given the responsibility of such sophisticated tasks as "lumbar puncture, peritoneal dialysis, cut-downs, funduscopic examination, and determine the severity of the hypertension just as easily as can the physician." Furthermore, the physician's assistant maintains that he can "feel the diastolic apical thrill, hear the opening snap after the aortic second sound and the diastolic apical rumble of the mitral stenosis, and make a diagnosis of mitral stenosis—when it has been previously overlooked by others;" and still more the responsibility of performing a highly technical task such as assisting with or actually "performing right heart catheterization—ordering the electrocardiogram —in addition making an accurate interpretation of it."

In doing research work on the dog he maintains that he can perform the anesthesia, and also "complete the entire experiment." So why *we* should bother to study diligently for 12 years and then have the physician's aide assume all the responsibility, while we sit in the office waiting for him to arrive and "do the histories, conduct the pre-employment examinations, sew up the minor lacerations, change the casts," etc., is a mystery. With all that, what is there left for the physician to do?

It is certain that we can utilize assistance in our practice, but the crying need for more "health care delivery" should not be allowed to abrogate high standards and sanction inferior medical service. It seems superfluous that we must now become so involved in establishing a whole new specialty which would involve legalities, new schools, curricula, teaching staff and the thousand-and-one other imponderables, when we have so close at hand nursing schools (male and female eligible) which are immediately available and could readily adjust to the training of young men and women to become "doctors' assistants" just as nurses have

*Lewis Cope, Minneapolis Tribune, Dec. 9, 1971.

always been or as we have trained them for our own use.* It is a disservice to the very honorable and efficient nursing schools and their profession to circumvent them. Their training program is infinitely better than the two-year program that is being designed for "assistant physicians."

Thirty years ago my associate and I trained, on the job, several graduate nurses to attend to the ancillary duties of taking preliminary histories and making preliminary rounds; starting intravenous fluids, drawing blood, collecting data, changing dressings, removing casts and taking out stitches; observing temperatures, pulse and blood pressure, and in general having vital signs and physical facts at their fingertips in order to assist us in discharging our own responsibility more efficiently. We also trained a few nurses to assist at surgery in the manner in which we wanted them to be our assistants. On no occasion would we have allowed anyone but a physician to assume the responsibility of "ordering medications, doing definitive physical and pelvic examinations, interpreting eye ground and cardiac murmurs; carrying out heart catheterizations, spinal punctures, peritoneal dialyses; suturing lacerations, putting on casts," and a host of other critical procedures that require the judgment of a fully-trained physician. These vital responsibilities have always been the trust of the physician and should continue to remain so.

Now, after a professional lifetime in the field of General Surgery, it seems that my generous heritage of good health has carried me full circle, for I clearly recall, before the First World War, as a young, eager, high school student, that my ambition was to go to the University of Valparaiso,† Indiana, where I could complete the entire medical training in two and one-half years. In my youthful enthusiasm, idealism and naivete, I visualized how wonderful it would be, at the end of that time, to start serving humanity.

But shortly after I had finished high school, and a couple of years in the A.E.F., World War I convinced me of the need for more education, not less; thereafter, at the end of 12 more years, I completed my medical and surgical training. Now, we are about to be relegated to the bleachers of the "clinical arena" to watch the latter-day barber surgeon take the spotlight in medicine that we had, half a century ago, so eagerly dreamed of achieving and maintaining. It seems that in our eagerness to satisfy the clamor of the numerous malcontents we are spawning a new profession that may prove to be more troublesome than some of the cults.

Carl O. Rice, M.D., Ph.D.
Editor Emeritus

*Heartily support Dr. Madeline Leiniger, Minneapolis Star, 8/10/72.
†Long since discontinued.

Dear Editor:

I am delighted that you published the wonderful manuscript entitled "The Development of Thoracic Surgery in the Upper Midwest" by Tom Kinsella as a supplement to the August, 1972 issue of MINNESOTA MEDICINE.

Tom was my student in Anatomy for a school year in 1915. At that time, I developed a high regard for him which has continued to the present moment.

When I published a multiple authored book in 1959, Tom's chapter on *Tumors of the Chest* was and is a classic. It was so excellent that I contacted the publisher Charles C. Thomas and recommended that it be reprinted in book form. Tom took great pride in that book.

In 1965 I suggested that he write the history of other phases of his chest surgery as he had done for tumors. He worked on this project until his death. I talked with him once after he entered St. Mary's hospital in November, 1969. He had taken a part of the manuscript to the hospital where he was putting in some finishing touches. However, when he died on November 12, 1969 some necessary work on the references remained. His long time excellent secretary Mrs. Florence Olson completed the manuscript.

The original of Kinsella's manuscript is on file in the University of Minnesota Library.

J. A. Myers, M.D.
Minneapolis, Minn.

The Viewing Box

Middle-Aged Woman with Dysphagia

EDWARD A. PETERSON, M.D.

THE PATIENT was a 47-year-old woman who entered the hospital complaining of dysphagia, weight loss, easy fatigability and vasospastic phenomena of the hands. She also had mild exertional dyspnea with slightly productive cough. X-ray examination of multiple systems disclosed many positive findings (Figures 1-5).

Diagnosis: Systemic scleroderma

Systemic scleroderma is of particular interest to the radiologist because of its many roentgenographic manifestations. The chief findings are as follows:

(1) The lungs show intermittent episodes of pneumonitis and pleuritis progressing to pulmonary fibrosis in the middle and lower thirds (Figure 1). This is interstitial in type.

(2) The heart shows non-specific enlargement of the cardiac shadow (Figure 1) with occasional pericardial effusion.

(3) Gastrointestinal tract has several manifestations. The esophagus is the most often affected. There is diffuse dilatation of the esophagus (Figure 2) with diminished or absent peristalsis. This is best seen in the recumbent position.



Fig. 1—Mild cardiac enlargement and fibrosis in basilar portions of both lungs.



Fig. 2—Esophagogram showing dilatation and diminished peristalsis of the esophagus.



Fig. 3—Small bowel study discloses dilatation of duodenum and jejunum.



Fig. 4—The barium enema reveals loss of haustration of the colon with some tendency to saccule formation.



Fig. 5—Wrist and hand: Decalcification of bones, soft tissue calcifications in the wrist and some absorption of distal ends of the terminal phalanges with adjacent calcification.

(4) Small bowel involvement is relatively common. Irregular areas of constriction and dilatation (Figure 3) are usually present with absence of mucosal pattern and delay in transit time.

(5) The colon has a bag-like appearance (Figure 4) with widemouthed saccules.

(6) The musculoskeletal system has rather characteristic features. There is tapering or absorption of the tips of the terminal phalanges (Figures 5) with multiple soft tissue calcifications (Figure 5) present in addition to periarticular soft tissue changes. Occasionally, large masses of calcification are seen about the joints, producing a so-called "tumoral calcinosis."

Request for Physican's Art Work

For many years the Board of Editors of MINNESOTA MEDICINE has recognized and supported photographic and other artistic talents of the members of the Minnesota State Medical Association publishing cover pictures in color of their work. Our series of color covers has received much favorable comment and many journals have followed us in the use of color art in this manner.

We solicit color photographs including pictures of all art forms created by members of the Association. These must be technically excellent to show off the subject to its best advantage.

Although in the past we have printed cover pictures depicting many distant parts of the world, photographs of life in Minnesota will be given preference. Because of limitation of space, pictures oriented horizontally are preferred. All pictures will be returned if identified with the name and address of the physician. Please submit your pictures as prospective cover subjects to the Editor of MINNESOTA MEDICINE, 375 Jackson St., St. Paul, Minnesota 55101.

Farrell Stiegler, M.D.
Cover Editor

New Director

Dr. George Mann has been named director of the Alcoholic Treatment Unit of St. Mary's Hospital, Minneapolis, and medical director of the Johnson Institute, an outpatient chemical rehabilitation center in Minneapolis.

Dr. Mann had been medical director of the St. Mary's unit since it opened with 16 beds in December, 1968. Now, as director of the 52-bed unit he is responsible for all phases of the two year, inpatient-outpatient, medically-oriented therapy and counseling program.

After receiving his M.D. in 1949 from Marquette University, Dr. Mann went into general practice until 1952 when he began a residency in anesthesiology at the University of Minnesota. He is certified by the American Board of Anesthesiology.

Procedures in Brief

Technique for Placing Umbilical Catheters

MARTHA BURKE-STRICKLAND, M.D.

THIS IS A PRESENTATION of technique only. Philosophy, uses and complications may be found in the listed references.

Precautions During the Procedure

During the procedure, monitor the infant's color, heart rate and respirations. Keep the baby warm. Maintain a rectal temperature of 37°C (98°F). Carry out the procedure within the incubator if a separate draft-free, thermistor-controlled heated work area is not available.

Work rapidly; prolonged procedures are extra stress for the baby. Properly organized, the complete procedure should not take more than ten minutes.

If the baby is in shock, cannulate the vein and initiate therapy before manipulating the arteries.

Maintain sterile technique.

Catheter Recommendations

A No. 5F blunted, open-end, radiopaque, polyvinal catheter* is suitable for most purposes. A No. 3F is available for use in infants weighing less than 1,000 grams. A No. 8F is available for exchange transfusions.†

Gavage feeding catheters are a poor substitute for umbilical catheters. The blind-end side hole predisposes to clotting; the side-hole is frequently occluded by arteriospasm; "adapting" the tube by cutting off the blind end leaves a sharp cutting edge that damages the vessel and increases risk of perforation.

Other Equipment

Set-up for the procedure should include adequate lighting, a Mayo stand, restraints for the baby, a constant infusion pump‡ if intravenous fluids are to be given, and a sterile umbilical tray.

The tray should contain:

—4 towels
—cotton balls
—gauze sponges
—2 curved mosquito hemostats
—1 thumb forcep
—7" straight jaw needle holder
—7" ring forceps
—2 5cc syringes
—1 oz. medicine cup filled with parenteral saline
—1 oz. medicine cup filled with Betadine
—curved cutting skin needle with 4-0 silk or woven nylon suture
—Bard-Parker handle with No. 11 blade
—5" straight scissors, blunt-sharp blades
—fine plain tip iris forceps —1 curve, 1 straight
—1 woven umbilical tape
—2 umbilical catheters
—2 disposable 3-way stopcocks

The capped end of the IV line should be readily accessible for attachment to the catheter when the latter is in place.

Safe restraints can be made by looping one end of a length of curlex gauze around the wrist or ankle. Tape in place to form a soft, snug bracelet, Position the extremity comfortably out of a field of action and secure by taping the free end of curlex to the incubator mattress frame.

Preliminary Procedure

The steps described are for working inside an incubator. Starred steps may be omitted if open facilities are used.

*Remove the iris covers from the portholes to facilitate sterile entry of the gloved hands.

The physician should scrub, put on sterile gloves and finish preparations for the procedure:

Assemble the Bard-Parker handle and blade, assemble needle and suture in needle holder, fill catheter with saline; leave catheter attached to syringe.

Place cotton balls in Betadine.

*Open one towel completely. Lay all instruments and supplies in the center. Fold the towel, envelope fashion, over the contents to make a spill-proof pack.

*While an assistant opens the access door to the incubator, place the pack over the lower ex-

Dr. Strickland is Director of Newborn Services, Hennepin County General Hospital, Minneapolis, Minnesota 55415.

*Argyle Umbilical Artery Catheter, Cit. #MAR 1602-5, Sherwood Medical Industries, Inc., St. Louis, MO.

†Pharmaseal Laboratories, Glendale, CA.

‡Harvard Apparatus, Millis, MA 02054.

See editorial, page 1015.

Suturing Umbilical Catheters

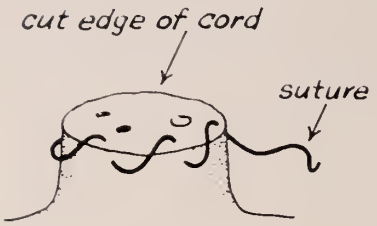


Figure 1. Overcast Stitch



Figure 2. Running Stitch

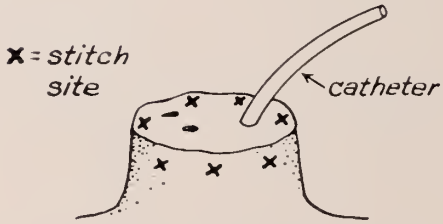


Figure 3. Suture Spacing

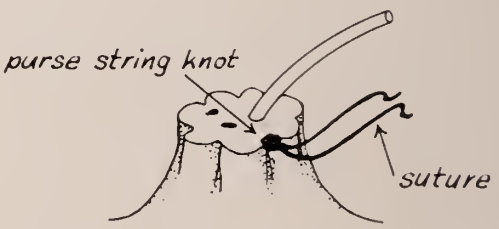


Figure 4. Purse String Suture Completed

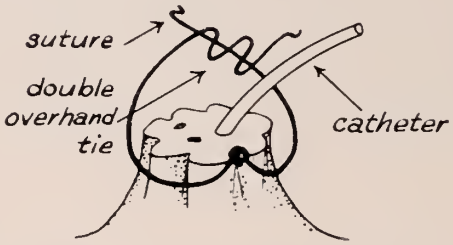


Figure 5. Double Overhand Tie Around Catheter

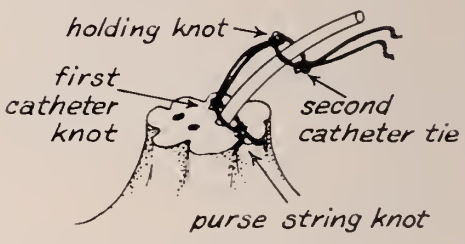


Figure 6. Completed Tie

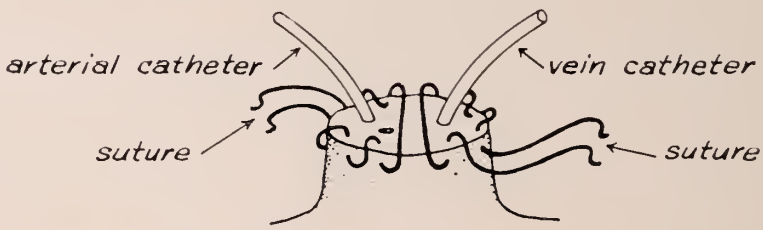


Figure 7. Separate Purse Strings for Arterial and Venous Catheters

tremities of the infant. The incubator is closed and the rest of the procedure is performed through the portholes. At this point, everything needed to complete the procedure should be inside the incubator. Avoid going in and out the portholes repeatedly.

Preparing the Site

Unfold the pack. While an assistant holds the cord stump off the abdomen, cleanse the stump and adjacent skin with Betadine. Avoid abrading the thin skin with rough scrubbing. Discard the used cotton balls and ring forceps away from the sterile area. Position the three towels to form a sterile field around the cord. Place the woven tape around the cord base in a single over hand tie to provide vessel control during the next step.

Use the Bard-Parker knife to sever the cord with a clean, even cut about ½ cm from the skin. Discard the remnant away from the sterile area.

Vessel Identification

Identify the arteries and vein with minimal manipulation of friable tissues. Remember that the vessels follow a spiral course through the cord. If the cord has been cut near the skin, the thin-walled, patulous oval lumen of the vein should be near the 12 o'clock position. The small, pinpoint lumina of the arteries should be seen jutting slightly above the surface of Wharton's jelly at 4 and 8 o'clock positions. If the infant is moribund, relaxed arterial lumina may be difficult to distinguish from the vein.

Catheter Insertion in the Vein

To cannulate the vein, remove any visible clot with a forceps, grasp the tissue near the vein with a curved mosquito hemostat, loosen the woven tape, quickly insert the catheter and advance to a premeasured length equal to the distance from the umbilicus to the xiphoid process. Retighten the woven tape. Keeping the vein occluded and using a saline filled catheter are essential for prevention of air embolism.

Obstructive kinks in the vein 1-2 cm beyond the abdominal wall may be overcome by exerting a steady, gentle pressure with the saline filled syringe as the catheter is advanced.

Rarely a problem at birth, obstructive clots encountered later may sometimes be removed by exerting a negative pressure with the syringe as the catheter is withdrawn. Clear the clot and reinsert the catheter. The risk of embolization or perforating the vessel is increased by forcing the catheter or pushing with a metal probe.

Position of Catheter in Vein

The catheter tip should lie in the inferior vena cava just about the diaphragm. If it cannot be advanced to this point, it may be left in the umbilical vein. The tip should not lie in the heart, the portal vein or branches of the hepatic vein. Check position with Xray before injecting hypertonic solutions.

In an emergency, insert the catheter only 1-2 cm for injection of medications. When the emergency is over, a new catheter can be placed in the desired position.

Cannulating the Artery

Catheterizing the spastic pinpoint lumen of an artery requires more skill. Stabilize the end of the artery by grasping adjacent tissue with a mosquito forceps. Insert the tip of the curved iris forceps into the lumen; allow the jaws of the forceps to open, exerting a gentle dilating pressure on the vessel. Insert the catheter tip between the jaws of the forceps. Continue to exert a steady, gentle pressure for 15-30 seconds. When the muscular spasm relaxes, the catheter begins to advance more freely. On rare occasion, injection of 0.1 cc of 1% Lidocaine may be needed to relieve the muscular spasm.

If the catheter will not negotiate the curve at the junction of the umbilical artery with the hypogastric artery after 30-60 seconds of gentle pressure or injection of the Lidocaine, try the other artery.

Advance the catheter a length equal to the distance from the umbilicus to the symphysis plus 3 cm. This will usually put the tip in the iliac artery. The catheter should not lie in the femoral artery nor adjacent to major visceral branches of the aorta. The catheter should be removed at once if there is unremitting vasospasm or other sign of disturbed circulation.

Securing the Catheters

If both arterial and venous catheters have been inserted, secure them with separate purse string sutures placed in the wall of the cord, not the skin. Snug the tissue up around the catheter and tie; wrap the suture around the catheter one time and tie again. Make a holding knot one cm beyond this, wrap the suture around the catheter

and tie again.

If only the vein has been cannulated, a single purse string suture should include the ends of the arteries to insure hemostasis.

An anchor suture in the wall of the cord with a tie around the catheter is not satisfactory for hemostasis nor prevention of air embolism around the catheter.

The woven tape should be removed from the base of the cord as soon as suturing is completed.

Tape the catheter to the abdominal wall with a ⅜″ x ¾″ strip of tape. Position so no torque pressure is exerted on the wall of the vessel. Tineture of benzoin to the skin before applying the tape improves holding and reduces skin irritation.

Dressings

No gauze dressings are used. Apply Neosporin and Myeostatin powder every four hours. Prevent inhalation of the powder by the baby. Creams and ointments are not recommended for use on the cord.

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Into the woods thenceforth in hast she went,
To seeke for hearbes, that mote him remedy;
For she of hearbes had great intendiment,
Taught of the Nymphe, which from her infancy
Her noureed had in trew Nobility:
There, whether it diuine *Tobacco* were,
Or *Panachaea,* or *Polygony,*
She found, and brought it to her patient deare
Who al this while lay bleeding out his hart-bloud neare.
The soueraigne weede betwixt two marbles plaine
She pownded small, and did in peeces bruze,
And then atweene her lilly handes twaine,
Into his wound the iuyee thereof did seruze,
And round about, as she could well it vse,
The flesh therewith she suppled and did steepe,
T'abate all spasme, and soke the swelling bruze,
And after hauing searcht the intuse deepe,
She with her searfe did bind the wound from eold to keepe.*

Edmund Spenser: Faerie Queene. Book III Canto V stanzas 32-33 (1590).

Cystic Fibrosis

Screen Newborn Infants

WARREN J. WARWICK, M.D.

LIFE TABLE STUDIES of the survival of different groups of patients with cystic fibrosis have shown a very poor prognosis without special treatment, a three-fold improved prognosis with special treatments, and an estimated ten-fold improvement with prophylactic pulmonary therapy.

Before 1939, when no effective treatments were known for cystic fibrosis, the survival curve for children with the disease was grave—only half of the children (97 diagnosed before 1939 and reported in the medical literature) were alive at eight months of age; only one-fourth were alive at one year, and only one was alive at age 10 years.[1]

After 1939 when antimicrobial drugs became available the survival curves showed half of the children still alive at 3½ years; one-fourth alive at nine years and about eight percent at 20 years.[2]

After the National Cystic Fibrosis Research Foundation started funding special Cystic Fibrosis Centers across the United States, prognosis improved even more. Throughout the United States the averaged survival for these children with cystic fibrosis reported from 78 Cystic Fibrosis Centers showed one-half still alive at 11 years and one-fourth alive at 20 years.[3]

These data also show that the interval from the age of diagnosis for children diagnosed between birth and 10 years of age to the death of one-half of the group was on the average 11½ years. This mortality pattern, that of an acquired disease, suggests that children with cystic fibrosis grow without special risks until some clinical pulmonary complication triggers a progressive destructive course.[3] These data support the thesis which prompted clinical study of a "prophylactic" approach to pulmonary therapy at the Western Reserve University.[4]

If prophylactic pulmonary therapy does prevent such a triggering event in the lungs, the remarkable survival curve achieved by Matthews, Doershuk and colleagues[4] is easy to understand. Their results, two-thirds of patients predicted to be alive at 19 years,[3] provide the best current argument for finding the child with undiagnosed cystic fibrosis before he develops symptoms.

How well are we doing? If the incidence of cystic fibrosis is near one case in every 1000 newborn infants, our data in Minnesota indicate that fewer than 20 percent of the cases are diagnosed. Because of this difference between predicted numbers and known prevalence, we planned a survey of 20,000 school children.

We rejected semi-quantitative tests such as the agar gell and the filter paper tests as inaccurate, we rejected pilocarpine iontophoresis as too slow, and we concentrated on a chloride-specific ion electrode test, using local heat as the sweating stimulus, because we had found the test to be as accurate as the pilocarpine test and very much faster.[5] In preliminary studies we could test at the rate of 150 patients per hour with a continuous assembly line mass production technique.

We tested 20,071 children in 26 cities around Minnesota. Their average age was eight years. We found only four patients, all previously known to their family doctor. This gave us a prevalence estimate of one case per 5,000 children aged eight years. Since only one-fourth of the patients with cystic fibrosis not receiving special therapy would be expected to live that long, we calculated an incidence estimate of one case in 1,200 newborn infants.[6]

Our conclusions were: (1) that the low prevalence of cystic fibrosis in school-aged children and the failure to find any undiagnosed cases were contraindications to mass screening of all school-aged children. (2) For such older children we recommend sweat testing if any of the cardinal

Research work reported in this paper was supported by a Cystic Fibrosis Care, Research, and Teaching Grant and Special Grants from the National Cystic Fibrosis Research Foundation and by special aid from the Minnesota Mrs. Jaycees.

Dr. Warwick is Associate Professor, Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota.

symptoms of cystic fibrosis appear. When all children with such symptoms are screened, about one child in 100 will be found to have symptomatic cystic fibrosis.[7] (3) That mass screening must be done at an age when most cases would be undiagnosed and when the results of therapy would be most effective, that is, in early infancy, preferably on the newborn infant.[8]

Since 1965 three techniques have been advocated for trials of newborn screening. One of these, a semi-quantitative estimation of the albumin content of meconium, has been adequately tested and discarded.[9]

The second, measurement of Na, K and Cl in the clipping of finger or toe nails by neutron activator and scintillation counting, has captured the imagination of many U.S. investigators because it can be automated and because there are enough neutron activators in the U.S. to test nail clippings from all newborns if the test proves successful.[10,11] At present the test is about 85% accurate for diagnosis of cystic fibrosis or diagnosis of normality; but it will require much more work to obtain an acceptable accuracy of 99 percent that can be achieved with conventional sweat tests.

The third approach is to do sweat tests on newborn infants. If such infants are hydrated and warm, adequate sweat can be obtained from them for *in situ* analysis with specific ion electrodes.

With our technique the sweat chloride values found after 24 hours of age are identical with the values we obtain on the same infants at three, six or nine months, at one to three years of age.

Pilocarpine iontophoresis can also be done; and if other simple fast reliable techniques for collection and analysis of sweat can be developed, either technique for screening newborn infants will be sufficiently accurate (99%) and simple enough for feasibility studies of newborn screening.[9]

Equipment is now available for a cooperative study between multiple hospitals to test 40,000 to 60,000 newborn infants.

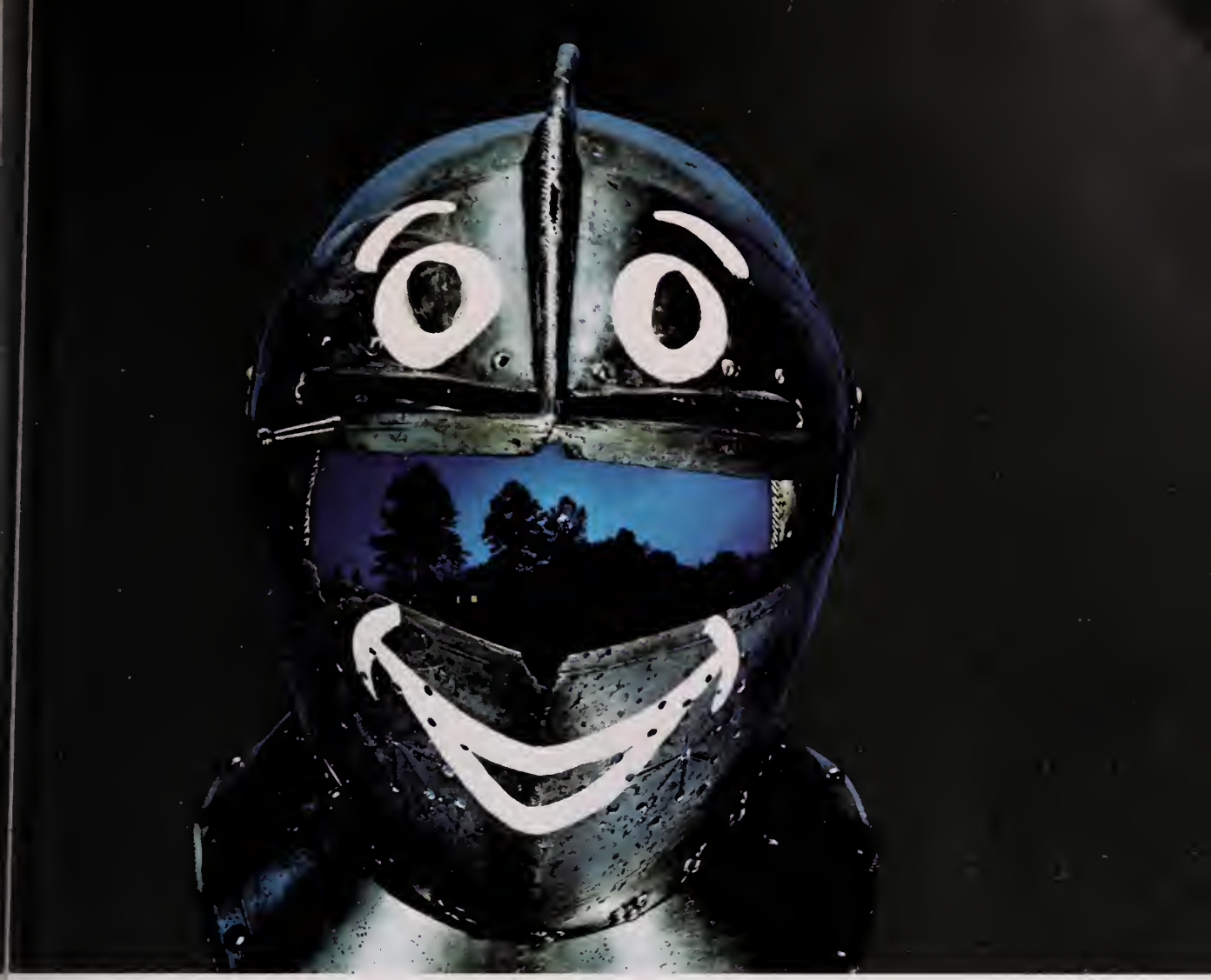
Summary

The grave prognosis for children with cystic fibrosis can be so improved with more intensive care, especially with prophylactic pulmonary therapy, that many such children can grow to be healthy adults. Screening programs are essential if the diagnosis is to be made prior to the development of unarrestable pulmonary complications. Screening programs for older children should be limited to children with any of the cardinal symptoms of cystic fibrosis. Mass screening of healthy children should be limited to the newborn period of early infancy. The sweat test can now be used to test the feasibility of eventual nation-wide newborn screening programs for cystic fibrosis.

A newborn screening program for cystic fibrosis ought to be started on a pilot scale because: (1) Early diagnosis and treatment can prevent the clinical complications; (2) Tests are available which will efficiently identify the one cystic fibrosis child from among the 1,200 normal newborns; (3) The cost of case finding is minimal compared to existing screening programs for phenylketonuria, and (4) The potential savings to the community through prevention of complications are very great.

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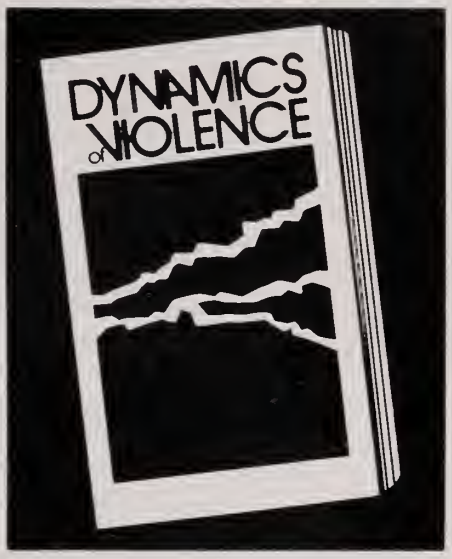
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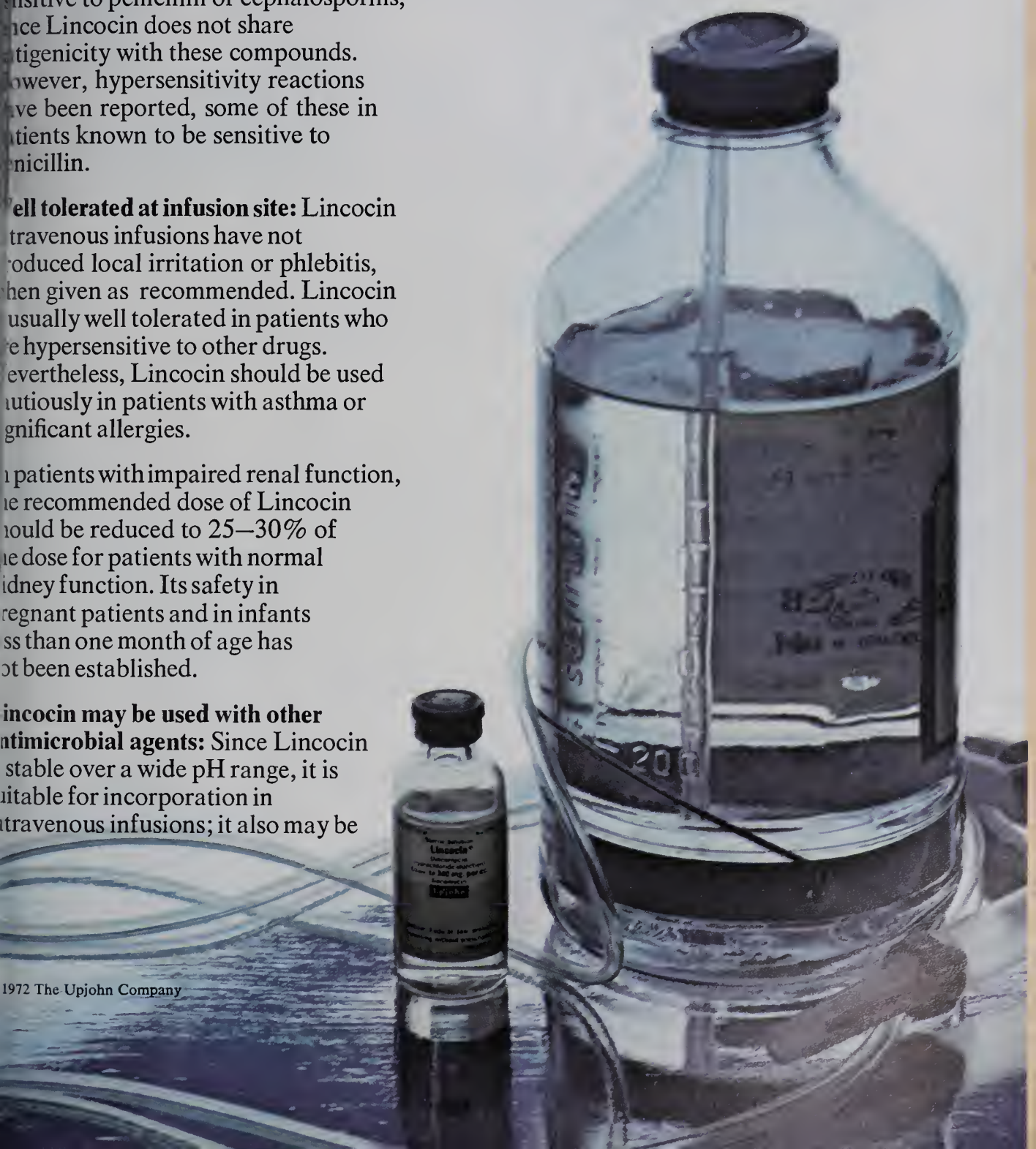
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Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatm *Skin and mucous membranes*—Skin ras urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis h been reported. *Liver*—Although no direc lationship to liver dysfunction is establis jaundice and abnormal liver function (particularly serum transaminase) have observed in a few instances. *Cardiovasc* —Instances of hypotension following pa teral administration have been repor particularly after too rapid IV admini tion. Rare instances of cardiopulmonary rest have been reported after too rapid administration. If 4.0 grams or more ad istered IV, dilute in 500 ml of fluid administer no faster than 100 ml per h *Special senses*—Tinnitus and vertigo h been reported occasionally. *Local react* —Excellent local tolerance demonstrate intramuscularly administered Linco (lincomycin hydrochloride). Reports of following injection have been infrequ Intravenous administration of Lincoci 250 to 500 ml of 5% glucose in dist water or normal saline has produced local irritation or phlebitis.

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Case Report

Concurrence of Achalasia

with Adenocarcinoma of the Stomach

REX B. SHAFER, M.D. AND JOHN R. JACOBSON, M.D.

Achalasia is a disorder of esophageal motility characterized by esophageal dilatation with absence of effective propulsive movements and failure of relaxation of the lower esophageal segment. The cause of achalasia is unknown, though many consider it to be of neural origin. Microscopic examination of the esophagus with achalasia reveals fewer ganglion cells than normal in Auerbach's plexus.[1-3] The reduction of ganglion cells is more pronounced in the body of the esophagus and to a lesser extent in the lower sphincter. The precise nature of the autonomic neural lesion has not been agreed upon.

Incidence

Carcinoma of the esophagus occurs with a definite increased incidence in patients with achalasia. This incidence of carcinoma has been reported to vary from one to 20%.[4-6] The most quoted incidence of 3% is probably accurate.[4] Histologically, squamous cell carcinoma has been found in essentially all instances. Only infrequently has adenocarcinoma been described, and then arising from the esophagus. The concurrence of achalasia with adenocarcinoma of the stomach is extremely rare.

Purpose

The following case is reported to re-emphasize the association of carcinoma with achalasia and more specifically to report the association of adenocarcinoma of the stomach with achalasia. Attention is drawn to the delay in recognition of the malignancy because of the presence of achalasia and its associated signs and symptoms.

From the Department of Medicine, University of Minnesota, Minneapolis, Minn., and Minneapolis Veterans Hospital, Minneapolis, Minnesota.

Reprint requests to Nuclear Medicine Service, Veterans Administration Hospital, Minneapolis, Minnesota 55417 (Dr. Shafer).

Case Report

A 40-year-old white male with a history of congenital achalasia, symptomatic since age six, was referred to the Minneapolis Veterans Administration Hospital because of abrupt onset of abdominal pain with melena and sudden hematemesis. History included the onset of substernal pain and difficulty swallowing at age six. Diagnosis of cardiospasm was made from the clinical history and typical x-ray changes.

Early Treatment

The patient was treated with dilatations which afforded little relief. He remained symptomatic through childhood, but learned to force food from the esophagus into the stomach by swallowing air. At age 20 he was re-evaluated at the Hines Veterans Administration Hospital and underwent an esophago-gastrostomy with a Heller myotomy.

He experienced significant clinical improvement and



Fig. 1—Barium swallow reveals dilated esophagus, showing typical conical narrowing of the lower segment.



Fig. 2—Upper gastrointestinal Xrays with contrast material in the dilated esophagus, shows filling defect (arrow) involving the cardia of the stomach.



Fig. 3—Gross autopsy specimen demonstrating: (1) dilated esophagus, (2) gastroesophageal junction, and (3) cardia and body of the stomach. The nodular serosa of the cardia of the stomach is identified (arrow).

remained asymptomatic until ten years later when he noted onset of gastrointestinal bleeding and melena. Esophagoscopy at that time demonstrated severe esophagitis. Surgery was recommended but was refused by the patient.

Present Illness

Conservative management with diet and dilatation was instituted. This therapy was reasonably effective until December, 1970 when at age 39 the patient experienced marked increase in dysphagia with associated 25 pound weight loss. In July, 1971, he was hospitalized at a local hospital where examination and biopsy of a supraclavicular lymph node established the diagnosis of metastatic adenocarcinoma. Esophagoscopy revealed a constriction of the lower esophagus near the gastrointestinal junction, with a fibrous mucosa which suggested carcinoma. The stomach was not entered. An upper gastrointestinal series was obtained and showed a mass involving the cardia of the stomach, as well as constriction and narrowing of the lower esophagus (Figure 1 and 2). Because of the obvious metastatic extension of the carcinoma, no surgery was performed. The patient was discharged and later admitted to this institution following the abrupt onset of abdominal pain and melena.

Physical and Laboratory Results

On presentation here, he was a pale, anxious white man with evidence of recent weight loss. Vital signs were unremarkable. A hard, nodular mass was present over the left supraclavicular area of previous biopsy scar. The liver was enlarged and palpable three finger-breadths below the right costal margin. The stool was guaiac positive. Laboratory values including a complete blood count, urinalysis, serum electrolytes and an SMA-12 survey were unremarkable except for an alkaline phosphatase of 65 King-Armstrong units (normal 4-17) and a serum glutamic-oxaloacetic transaminase of 300 Babson units (normal 10-40).

Management and Course

Initially, the patient's gastrointestinal bleeding was managed with intravenous hydration, nasogastric suction, and gastric lavage. The patient was treated symptomatically. He died after twelve days in the hospital.

Autopsy

At postmortem examination, the esophagus was dilated throughout its entirety, measuring six cm in diameter at its mid-portion. Immediately above the gastro-esophageal junction, there was focal thickening with a ragged mucosa, but no ulceration or infiltration of the esophageal wall. The esophagogastric lumen was markedly narrowed and two tracts passed from the esophagus into the stomach. The cardia of the stomach was thickened with nodular serosa, the largest nodule of which measured four cm in greatest dimension (Figure 3). The lungs, liver and mediastinal lymph nodes were all grossly involved with tumor. The liver was large, extending eight cm above the xiphoid and seven cm below the right costal margin, and there were numerous nodules present on its surface. Histologic sections of the tumor from the cardia of the stomach, lungs, liver and medias-

ial nodes all contained undifferentiated adenocarcinoma (Figure 4).

Discussion

Thomas Willis first reported achalasia in 1679.[7] n 1872 Fagge described a patient with carcinoma eveloping in a dilated esophagus presumed to be halasia.[8] Since then, there have been numerous oradic case reports of the coexistence of carnoma and achalasia. Unfortunately, disparate gures persist regarding the exact incidence of is association. In a most recent review of the bject by Just-Viera and Haight in 1969, a total f 167 patients with achalasia and carcinoma ere reviewed.[4] This represents a summation of ne reported world's literature.

The incidence of the coexistence of achalasia nd carcinoma of the esophagus has been reported o be from 1 to 20%. The usual figure of 3% or the incidence of the coexistence of these two liseases seems reasonable.[4,5] This figure is dependent upon the duration of follow-up observation because carcinoma does not develop until nany years after the onset of symptoms and diagnosis of achalasia. Williams reported an average apse time of 18 years between the onset of symptoms due to achalasia and carcinoma detection.[9] In some instances this interval has been as long as forty years. For this reason, a series weighted with patients having achalasia for a much longer duration would show a higher incidence of carcinoma.

Squamous Cell vs. Adenocarcinoma

Most reports incriminate squamous cell carcinoma of the esophagus as the most common malignant tumor accompanying achalasia.[4-6,10] Only a single example of adenocarcinoma localized to the cardia of the stomach was included in the review of Just-Viera and Haight.[4] This histological type is only infrequently associated with achalasia because the predominant primary site of the neoplasm is the esophagus, not the stomach.

Theories

There have been multiple theories proposed as to why achalasia might predispose to malignancy. Fleiner initially suggested that the trauma of repeated tube bouginage in patients with achalasia might lead to the malignant transformation.[11] Rake postulated that the carcinomatous transformation seen may result from necrotic irritation of the esophageal mucosa caused by retained foodstuffs and saliva.[12] He drew the comparison of this process to the malignant transformations seen in patients with long-standing ulcerative colitis. Virno and Carboni reinforced the belief of most authors supporting the view that carcinoma is a result of local chronic irritation that is present in achalasia.[13] They proposed that an initial stage of muscular hypertrophy was seen early in the disease which subsequently was followed by esophageal dilatation and then retention of the esophageal contents. This resulted in a change in the character of the esophageal wall, which permitted increased bacterial growth and continuous

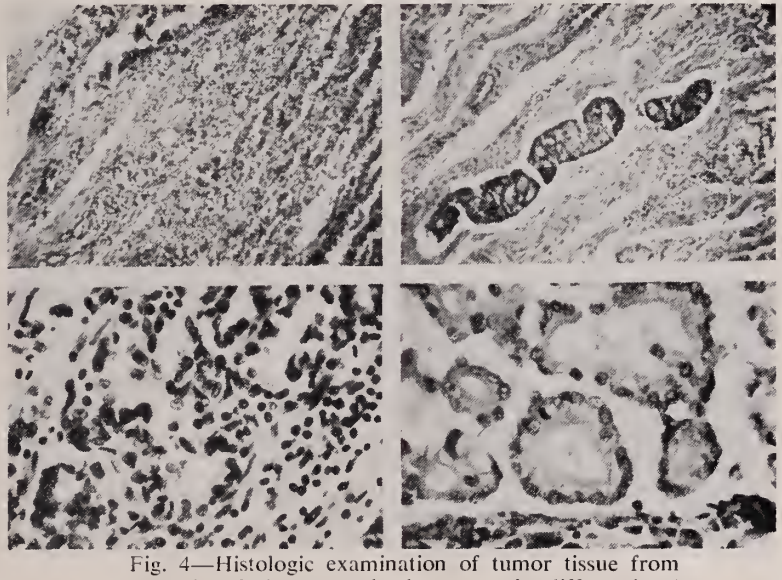


Fig. 4—Histologic examination of tumor tissue from the cardia of the stomach shows poorly differentiated adenocarcinoma.

chemical irritation from retained, decomposing food. The resultant chronic esophagitis then becomes the fertile ground for metaplasia of the epithelium to occur. Neither the trauma of repeated bouginage or the chronic irritation caused by retained foods could be implicated logically in the association of achalasia with adenocarcinoma of the cardia of the stomach. The same motility dysfunction involving the esophagus may also have involved the epithelium of the gastric cardia.

Management

If these theories are correct and stasis and chronic irritation contribute to the incidence of malignant degeneration, then prompt management eliminating stasis would reduce the occurrence of carcinoma. The findings reported by Wychulis et al. from the Mayo Clinic support the impression that there is reduced incidence of carcinoma in patients who have had early surgical treatment by esophagogastric myotomy.[6] This results in a more effective prophylactic measure to control retention of esophagitis and it is believed by them to reduce the incidence of premalignant changes. Le Roux and Wright refute this point and feel that if the drainage procedure is not complete, the potential for development of carcinoma may be even greater.[14]

The consensus of opinion from the literature then is that if early and adequate surgical intervention is performed and the patient is relieved of symptoms, there is probably a reduction in the incidence of carcinoma. In our patient there was a 20-year interval after his Heller myotomy before the diagnosis of carcinoma, although he had been symptomatic for the ten years prior to this diagnosis.

Recognition of the malignant potential in a patient with achalasia demands that he have regular, periodic examinations. There exists at lea three reasons for delay in recognition of mali nancy in the patient with achalasia: (1) the patie with achalasia is already accustomed to episod of dysphagia and with the onset or recurrence this symptom, he does not seek early medical a tention, (2) there is difficulty in x-ray diagnosis the malignant lesion because of the long-standir changes of achalasia and possible previous oper tive procedures, and (3) because of the dilat cardio-esophageal junction, considerable extensic of the malignancy has to occur before there obstruction of the lower esophagus and seriou symptoms of dysphagia with regurgitation.

Conclusion

While the co-existence of achalasia with squan ous cell carcinoma of the esophagus has been r ported, the concurrence of achalasia and carcin ma of the stomach is extremely rare. Similarit in etiology including race, age and duration symptoms are common to both malignant lesion Whether relief of stasis by an esophageal myotom delays malignant degeneration, or whether the d generation occurs as a natural sequence of th lesion is unknown. Certainly, the difficulty i early diagnosis of malignant change was compl cated by the previous diagnosis of achalasia. Be cause of recurrent episodes of dysphagia, the pa tient did not seek early medical advice. Onc examined, the dilated cardio-esophageal junctio was not initially interpreted as malignant becaus of the changes of achalasia and previous surgica intervention. Finally, demonstration of a malig nant mass involving the cardia of the stomach wa accomplished by x-ray diagnosis, esophagoscop gastroscopy and biopsy.

Acknowledgment

Pathological material was kindly supplied by Paul F Nordlie, M.D.

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Fracture Conference

The Thumb Metacarpophalangeal Joint

Injuries

RONALD L. LINSCHEID, M.D., R. WAYNE GRAINGER, M.D. AND
EINER W. JOHNSON, JR., M.D.

Dr. Wayne Grainger:

This conference is concerned with injuries to the ligaments of the metacarpophalangeal joint of the thumb. Stability of this joint depends on the radial and ulnar collateral ligaments which run from the first metacarpal to the proximal phalanx. A force deviating the phalanx ulnarly or radially may tear the ligament on the opposite side or avulse its bony attachment. If the injury is ignored or treated improperly, instability of the metacarpophalangeal joint results, producing pain and weakness on pinching motion of the thumb.

The first patient was a 22-year-old nurse who dislocated the metacarpophalangeal joint of her right thumb while skiing, and this was reportedly reduced by the ski patrol at the site. When she was seen here, she had tenderness, swelling, ecchymosis, and slight radial deviation of the metacarpophalangeal joint. Figure 1 shows the roentgenogram made about 36 hours after the injury.

Dr. Wayne E. Janda:

There is a slightly displaced avulsion fracture at the ulnovolar aspect of the proximal phalanx of the thumb. This is presumably from an abduction sprain of the joint and may indicate injury to the ulnar collateral ligament or its insertion. There is also a suggestion of volar subluxation of the joint.

Dr. Grainger:

The second patient was a 35-year-old male physician who sustained a dislocation of the metacarpophalangeal joint of the thumb when the starting cord of his lawn mower flew back and twisted his thumb. He noted then that *at that time* his thumb was in slight ulnar deviation at the metacarpophalangeal joint. Figure 2 shows the roentgenogram made when he was seen here.

Dr. Matko Milicic:

There is ulnar deviation of the proximal phalanx. I would suspect that the radial collateral ligament has been injured. The injured collateral ligament might be repaired to ensure adequate reduction and late stability, although casting for four weeks is an acceptable alternative.



Fig. 1 (Case 1)—Postreduction film of 22-year-old nurse who dislocated thumb metacarpophalangeal joint, showing avulsion of small articular fragment with insertion of ulnar collateral ligament. Slight volar subluxation persists.

Drs. Linscheid and Johnson are in the Section of Orthopedic Surgery, Mayo Clinic and Mayo Foundation.
Dr. Grainger is a Resident in Orthopedic Surgery, Mayo Graduate School of Medicine (University of Minnesota), Rochester.
Fracture Conference, May 12, 1969.

Dr. Grainger:

Does the roentgenographic appearance make any difference in your proposed treatment?

Dr. Milicic:

The physical examination to assess unusual mobility at the joint is as important as the roentgenogram. Stress roentgenograms should be made of both thumbs to demonstrate the degree of ligamentous laxity or rupture. Local anesthetic instilled sterilely into the joint may be necessary to achieve this. There is also an obvious small avulsion fracture on the ulnar aspect of the joint, which appears to be a margin of joint surface avulsed with the dislocation. In this instance, however, this is of less importance than the radial collateral ligament injury.

Dr. Grainger:

In both instances the thumb was deviated to relax the involved ligament, and small gauntlet casts were applied. The first patient, the nurse, wore the cast for three weeks. She was seen one week after cast removal and had satisfactory maintenance of the reduced position and good stability and pinch without pain. The second patient managed himself and was lost to follow-up. We will have to get the follow-up from Dr. Linscheid.

Dr. Ronald Linscheid:

He has a stable, painless thumb and is doing very well. Injury to the ulnar collateral ligament may represent a partial tear or a complete rupture. A distinction should be made because open reduction is indicated in the latter case. The necessity of this has been explained and emphasized by Stener.[1] When the ulnar collateral ligament is torn by marked radial deviation, the avulsion occurs at the insertion at the base of the proximal phalanx. The proximal margin of the extensor mechanism is pulled distally with the thumb and slides over the raw end of the collateral ligament. When the thumb recoils, the extensor margin retracts the ligament away from the site of avulsion. Thus prevented from spontaneous healing, the joint remains unstable and insecure.

Dr. Mark B. Coventry:

Last month I saw a patient, a man about 23 years old, with this deformity untreated initially and with marked disability with relaxation of the metacarpophalangeal joint of the thumb. Not knowing what else to do, we decided to perform arthrodesis of the joint. He was a student, and even holding a pen to write his examination pap was painful and difficult. Another patient wi similar history and findings had been treated the same fashion several years before. I presun from my experience with two cases that it is muc



Fig. 2—(Case 2)—Self-reduced subluxation of thum metacarpophalangeal joint. Despite fragment of bone o ulnar margin of joint, there was ulnar deviation o thumb, tenderness, and instability of radial collateral lig ament.

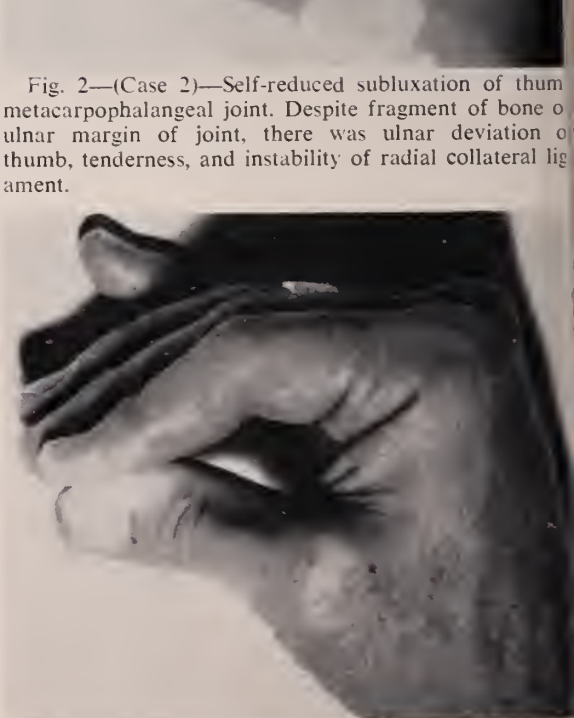


Fig. 3—Unstable ulnar collateral ligament in 33-year old orthopedist.

better to treat these positively and adequately rather than as late complications.

Dr. Linscheid:

We do not commonly see this injury. An unstable thumb may result when either the radial or the ulnar collateral ligament of the metacarpophalangeal joint is sufficiently injured, although the latter is of greater significance.

Dr. Grainger:

My own thumb was treated conservatively 13 years ago. I wish it had been operated on. It is unstable (Figure 3) and has been a nuisance, especially in doing fracture manipulations.

Dr. Edward M. Tapper:

The same injury in a younger person produces an epiphyseal separation rather than a collateral ligament rupture.

Dr. Linscheid:

We were just going to show that. A 12-year-old girl with hypermobile joints sprained her thumb while turning cartwheels. A stress view of the thumb is shown in Figure 4. There was point tenderness directly over the ulnar collateral ligament, and radial abduction was significantly greater in the injured than in the noninjured thumb. Dr. Dobyns explored this injury and found a type I epiphyseal fracture: a fracture entirely through the cartilaginous portion of the growth plate. Healing was uneventful with cast fixation. I apparently did not stress this thumb sufficiently to demonstrate it on the roentgenogram.

Dr. Tapper: This is a common skiing injury.

Dr. Linscheid:

Yes. When skiers slip a hand through the wrist strap to grasp the pole, many tend to twist the strap around the radial border of the thumb. Thus, if they fall, the strap tends to adduct the thumb ulnarly over the handle of the pole or may act as a fulcrum to the radial aspect and aid ulnar collateral ligament injury. Soreness of this joint is extremely common in skiers.

Dr. James H. Dobyns:

Water-skiing is an even more significant cause of serious injury to the thumb; I have seen three thumbs completely avulsed by the tow rope. I favor aggressive treatment in the matter of sprains. Flexibility of the thumb at the metacarpophalangeal joint is not nearly as important as stability of the thumb at this joint. I agree with Dr. Coventry; one sees many patients with thumbs disabled by injuries that produce instability and weakness because of rupture of the collateral ligaments.



Fig. 4 (Case 3)—Type I epiphyseal separation in 12-year-old girl. Torn ulnar collateral ligament was suspected. Stress film failed to open the epiphyseal separation which was obvious at operation.

Dr. Linscheid:

These three cases illustrate the effect of a force that deviates the phalanx from the long axis of the metacarpal of the thumb. After epiphyseal closure, rupture of one of the collateral ligaments results. If left untreated, these thumbs are weak, unstable, painful, and disabling. Often, arthrodesis of the joint is the only subsequent treatment left.

We believe that vigorous initial treatment is indicated. In some instances this means open reduction and accurate replacement or repair of the avulsed or parted ligament. With lesser injuries, reduction and casting are sufficient. Adequate fixation for the necessary time is also an

important factor, with a minimum of three weeks.

Prior to epiphyseal closure, separation of the proximal phalangeal epiphysis often results from this same force. Manipulative reduction is most often the successful means of treatment.

References

1. Stener B: Displacement of the ruptured ulnar collateral ligament of the metacarpo-phalangeal joint of the thumb: a clinical and anatomical study. J Bone Joint Surg [Brit] 44:869, 1962.

Historic Hospitals

Arab Hospital Architecture



Courtyard of the Nuri Hospital at Damascus, built in the twelfth century. Herzfeld, Ars Islamica, IX: 1, 1942.

The Arabs built their early hospitals in population centers for maximum availability to the people. They conceived of hospitals as refuges from the crowding of the surrounding city where the sick could find peace and comfort as well as treatment. The central courtyard, the most characteristic architectural feature, was said to be modelled after the Prophet's simple home at Medina. Mohammed's advice against elaborate and costly buildings was widely disregarded, however, as ambitious builders produced structures of ever greater dimensions and more grandiose conception.

The first of their hospitals was built at Baghdad of sun-dried mud brick. As the center of the culture shifted to Damascus and Cairo the humble material gave way to limestone, granite, and marble. The typical floor plan consisted of four high-ceilinged arcades arranged in the form of a cross with the courtyard at its center. Each arcade, open on the side facing the courtyard, was subdivided into rooms, or iwans, used for wards, examining rooms, and the many special purposes required by a hospital. The complex subdivision made it possible to segregate the patients by sex and by the nature of their disease. In the late Middle Ages the specialized wards were attended by physicians of appropriately specialized training and interest.

Many of the arcades included fountains with running water draining by aqueducts into the pool at the center of the courtyard. Because of their desert origin the Arabs found special comfort and security in freely flowing water; even the earliest Baghdad hospitals made use of its esthetic value and cooling effect. In colder regions such as Anatolia the same general plan was followed except that the central courtyard was covered over by a vaulted masonry ceiling.

Warren L. Kump, M.D.
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Alcoholism

Hospital Treatment of Alcoholism

A New Therapeutic Concept

GEORGE MANN, M.D.

We in the medical profession hold the philosophic attitude that we will care for all persons who have medical problems regardless of their nature. Persons with certain illnesses, however, have a difficult time receiving medical care. The alcoholic clearly exemplifies this defect in medical care. His disease is destructive to himself, his family, and his social environment.

Three years ago, we at St. Mary's Hospital decided to try to help the individual and society by providing care for the alcoholic. We wanted to show that a private general community hospital could effectively care for and rehabilitate alcoholics. Alcoholics are ubiquitous in our hospital population. Traditionally we treat alcohol complications in medical and surgical units. The emotional complications have been treated in our psychiatric units.

But nowhere in the general hospital has it been possible for the alcoholic to receive care for the etiologic process that produces these complications. Our basic premise is this: alcoholism can be diagnosed in its early stages and proper therapeutic and rehabilitative efforts can be made to forestall medical complications and to return the alcoholic to society as a functioning responsible person. Our present system of medical education largely ignores this concept of the disease. There is extensive information available to the student in diagnosing and treating alcohol-caused problems of the liver, pancreas, brain, etc., but little didactic or clinical experience in the basic disease process. As a result the focus in medicine today is not on early diagnosis and treatment, but rather on relief of symptoms and therapy for complications.

Dr. Mann is Medical Director, Alcoholism Unit, St. Mary's Hospital, Minneapolis, Minnesota. (Also see page 1020.)

Given as part of a Symposium on the "Treatment of the Hospitalized Alcoholic" which was presented to the combined meeting of the Mayo Clinic Staff and the Zumbro Valley Medical Society on November 4, 1970.

The general community hospital possesses within its institutional structure individuals who can be used effectively in the care of the alcoholic patient. For these people to use their backgrounds efficiently it is necessary to add to the hospital staff others who are expert in the general field of alcoholism and chemical dependency. They can act in ways that enable others in the hospital to focus on this process in a more realistic way than has been done traditionally.

The alcoholic has developed a pattern that affects him in most vital areas of his existence. He must be considered as an individual who is sick physically, emotionally, intellectually, socially, and spiritually. This process envelops the entire human being.

In order, then, to restore this individual to a functional level, therapy must be directed to all five of these areas—hence, the concept of a multidisciplinary approach to treatment. It is our belief that the patient has the best opportunity to achieve the necessary goals for his rehabilitation when the medical staff, nursing staff, counseling staff, clergy, dedicated laymen, and recovered alcoholics all function together in a spirit of equality and teamwork.

There is embodied in the previous statement the concept upon which effective treatment in this area pivots. This concept is that the traditional lines of authority and classic ways of communicating within the hospital structure must be altered. The multidisciplinary approach dictates that professional, paraprofessional, clerical, and lay therapists must all assume co-responsibility, for the overall good of the patient.

We physicians seem to be one of the most conservative groups in our society. The alteration of this way of behaving entails a change of attitude and a willingness to risk some personal involvement with persons who have not yet been included in the spectrum of professionalism in other areas.

I cannot emphasize too strongly the need for the production of an environment which will provide the staff with the greatest degree of freedom to act responsibly and to communicate with each other on an open peer level.

Results

The only way a unit such as ours can justify its existence is by objectively reporting the positive results of such a program. At this point we have been treating patients for two years. Our results are as follows: about 60% of our patients, upon completion of their inhospital therapy, move into our outpatient program, become involved with Alcoholics Anonymous, and stay sober. About 20% of the patients experiment one or more times with alcohol or drugs for relatively brief periods of time, but remain involved in the outpatient program and continue to make efforts to alter their behavior patterns and become more responsible. The remaining 20% lapse into their old behavior patterns, but even among these, because of their experience in treatment and their families' experience in what can be done with others, a high percentage are returned for subsequent treatment either to our hospital or some other institution for therapy.

High on the list of beneficial results must be placed the help that is afforded the family of the patient, whether the patient is able to achieve independence from chemicals or not. In many cases, for the first time in years, the family develops insight into the alcoholic and also an understanding of the role that they play in this disease process. Another great therapeutic result we see is that almost 90% of our outpatients are returned to productive employment or resumption of interrupted educational processes. The ultimate benefit of this to the community cannot be estimated.

At this time we have treated 559 patients; although this is not a great number compared to the estimated 60,000 alcoholics in Hennepin County alone, it is a sufficient number to conclude that the efforts being made in our unit can produce an impact in our community that will be beneficial in areas of employment, traffic accidents, legal procedures, divorce, delinquency, financial stability, community responsibility and other areas that are eroded by this destructive disease process known as alcoholism.

Crippled Children Services

Multidisciplinary Workshops—1972-73

The following Workshops have been arranged for physicians, nurses, teachers, psychologists, speech therapists, social workers and others working with children with a handicap.

No registration fee will be charged. Registration is at 8:30 a.m. unless specified.

Learning Disabilities

A panel consisting of a pediatric neurologist, occupational therapist, speech pathologist and clinical psychologist will discuss the evaluation and treatment of children with learning disabilities.

Various tests and procedures used to identify and evaluate children with learning difficulties will be discusssed by each discipline. Suggestions will be provided for helping a learning disabled child function in a regular classroom. Actual cases will be staffed by the team and there will also be an opportunity for small group discussion with each discipline.

November 3, 1972	St. Cloud	St. Cloud State College Atwood Memorial College Center
December 15, 1972	Winona	Winona State College Kryzsko Commons
Early 1973	Fergus Falls; Willmar; Marshall; Mankato; Hibbing	

Verapamil

An Anti-anginal Agent

RICHARD R. MOYER, M.D.

AN ORIGINAL PROTOCOL was designed and followed in an attempt to evaluate the therapeutic value of verapamil in a double-blind clinical trial.

Verapamil is α-isopropyl-α-S-(N-methyl-N-homo-veratryl)-α-aminopropyl)-3, 4-dimethoxyphenylacetonitrile and has the structural formula shown in the Figure.

Haas and Hartfelder found the following pharmacologic effects in dogs in lower doses: (1) increased coronary blood flow; (2) increased oxygen saturation of coronary sinus blood with decreased cardiac arteriovenous oxygen differences; (3) variable changes in 0_2 uptake by myocardium.[1]

Higher doses caused lowering of arterial pressure, bradycardia, and decreased myocardial contractility. The difference between the therapeutic and toxic doses was wide. Clinical reports have indicated that verapamil is effective in the treatment of angina.[2]

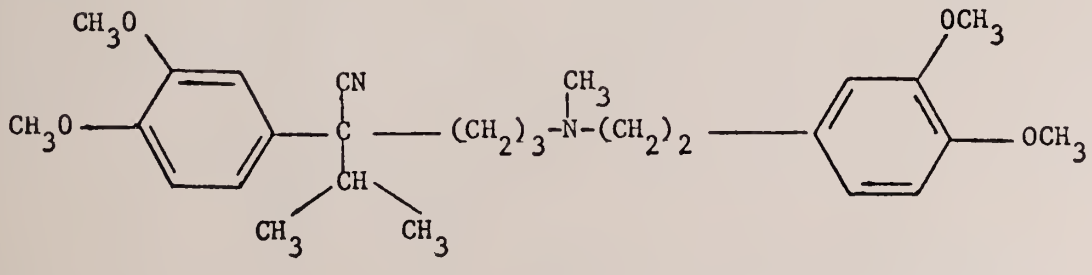
Method of Study

After a one month rapport single-blind period, a double-blind crossover study was performed to determine the efficacy of verapamil hydrochloride (80mg) in comparison with placebo, in reducing the frequency of reported attacks of exertional angina and nitroglycerin tablets required for its relief. Each patient acted as his own control. The same kind and number of observations were made both in the drug and in the control periods and for the same duration.

Cooperative patients, with objective criteria confirming the diagnosis of angina pectoris (characteristic symptoms plus positive double Master's two-step test, documented history of myocardial infarction, coronary angiogram, or characteristic resting electrocardiogram) with more than five attacks per week, volunteered to participate in this study. Patients who improved by more than 50% reduction in number of attacks while on placebo during the initial rapport period and patients who did not improve on nitroglycerin were rejected from the study. Patients receiving other experimental drugs or experimental therapies for angina or other conditions were excluded.

Twenty-five patients with confirmed angina pectoris secondary to documented coronary arteriosclerosis were studied. In the classification of the New York Heart Association, all were graded Functional Class III (marked limitation of physical activity) or Class IV (inability to carry on any physical activity without discomfort). Patients with angina due to other causes, e.g. aortic stenosis and insufficiency, or arteriovenous fistula were not included in this study. Coronary arteriosclerosis complicated by systemic hypertension in excess of 110 mm HG diastolic was excluded. Patients with

Dr. Moyer is associated with the Mesaba Clinic, Hibbing, Minnesota.



Figure

other systemic diseases which would make the interpretation of the pain difficult—as angina associated with gallbladder stones, hiatus hernia, or duodenal ulcer—were rejected. Patients with depressed sensorium due to narcotics, sedatives, or tranquilizers were excluded. There was no upper age limit, but patients with severe cerebrovascular disease and chronic brain syndrome were excluded because in such patients the evaluation of the anginal response to therapy is difficult.

The frequency of attacks of anginal pain and the number of nitroglycerine tablets required to remain comfortable (not symptom-free) were counted. Other non-quantitative characteristics of angina such as changes in character, intensity, exercise tolerance, and anatomic distribution were also evaluated. Any changes in the patient's emotional state, environment, marital, or occupational status which accounted for a change in the patient's angina were recorded. Efficacy was assessed by statistically significant quantitative changes or consistent subjective improvement affecting the clinical picture of the disease.

Results

Twenty-five patients with angina pectoris due to arteriosclerosis and who had evidence of a previous myocardial infarction were studied. Fourteen were male and eleven were female. The mean age was 63.8 years and the range was 45 to 91 years. The dose of verapamil was 80 mg q.i.d.

Minor adverse reactions occurred in nine of the patients while on verapamil and three of the patients while on placebo. In no instance was the drug discontinued because of side effects. Constipation, dizziness, headache, urinary frequency, and gaseous distention were the symptoms noted during the verapamil period.

No laboratory abnormalities occurred that were considered to be drug related.

Discussion

A striking early improvement (usually on the first day) was noted by most patients on verapamil. In addition to a sharp curtailment in the number of anginal attacks and a reduced need for nitroglycerin, many patients noted a sense of well being with a desire and ability to be more active. Because of this, the numerical data do not fully show the clinical effects of the drug. Many patients found they were able to perform work (such as shoveling snow, mowing lawns, etc.) which they were unable to do during the baseline or placebo period. This added work may have maintained the attack rate. A variety of other drugs previously given to these patients were continued during the study period without any unusual effects. These include: anticoagulants, hypoglycemic agents, thiazide diurectics, antidepressants and tranquilizers.

A further indication of the measure of benefit derived from verapamil can be obtained from the fact that, despite the inconvenience of repeated laboratory and clinical evaluation necessary during the experimental study, all patients wished to continue with verapamil.

Results

The raw data from this study consisted of three measures. Each patient reported the number of exertional angina attacks, the number of nonexertional angina attacks, and nitroglycerine tablets taken between visits. Patients were examined at 14-day intervals. Two observations were made at baseline while the patients were known by the investigator to be on placebo. Thereafter, each patient was placed in a double-blind fashion on either verapamil or placebo for five visits then crossed over to the alternate drug for another five visits.

Each measure was analyzed three ways. Verapamil was considered effective if each number of episodes of angina the patient experienced while on verapamil was less or equal to the smallest number recorded while the patient was on placebo, or if the number recorded while the patient was on placebo was greater than or equal to the greatest number recorded while the patient was on verapamil. This method of analysis tends to downgrade the effect of verapamil by failing to consider

TABLE 1
Sign Test on Number of Patients with Unambiguous Differences in Response

	Extertional Attack	Non-Exertional Attack	TNG Tablets
Number of Patients	11	10	8
Number of these who improved on verapamil	10	5	7
SignTest Significance Level	0.006	7.17	0.035

marginal cases. The number who appeared better on verapamil were subjected to a sign test. The results are displayed in Table 1, indicating significant improvement under verapamil for exertional attacks and for the number of nitroglycerine tablets.

For the second method, baseline averages were calculated for each patient on each measure. Each recorded value was then converted to percentages of baseline. Mean percentages for verapamil and for placebo were then subjected to a paired t test. The results indicate significant improvement of exertional attacks and for nitroglycerine consumption.

Finally, the differences between the observed value and the baseline were compared by the mean sign test (Table 3).

By all three methods of analysis, verapamil decreased both the number of exertional attacks of angina pectoris and the number of nitroglycerine tablets taken.

Conclusion

Verapamil at a dose of 80 mg q.i.d. (320 mg per day) effectively decreases the frequency of angina pectoris due to coronary artery disease. Drug side effects included constipation and dysuria and were mild in severity.

Acknowledgment

The verapamil and an identical appearing placebo were made available by Chas. Pfizer & Co., Inc., & Knoll Pharmaceutical. I would like to thank Dr. Kenneth Ahola, Angeline Johnson, R.N., Antoinette Mestnick, R.N., and Darla Willmarth, L.P.N. for their assistance in the study.

TABLE 2
Paired t Tests on Mean Percentages of Baseline

	Exertional Attack	Non-Exertional Attack	TNG Tablets
Mean Difference	48%	67.9%	40.6%
t Statistic	2.831	1.442	2.839
d of f	23	21	23
Significance Level	<.005	0.08	<.005

TABLE 3
Sign Test on Mean Percentage Differences

	Exertional Attack	Non-Exertional Attacks	TNG Tablets
Number of Patients with Differences	24	21	24
Number better on verapamil	18	14	18
Sign Test Significance Level	0.011	0.095	0.011

References

1. Haas H and Hartfelder G: α-Isopropyl-α-[N-methyl-N-homoveratryl)-μ-aminopropyl]-3, 4-dimethozyphenyl-acetonitril, eine Substanz mit coronargefasserweiternden Eigenschaften. Arznei-Forsch 12:549, 1962.

2. Sandler G, Clayton GA, Thornicroft SG: Clinical evaluation of verapamil in angina pectoris. Brit Med J 111: 224, 1968.

Macbeth: Canst thou not minister to a mind diseased,
Pluck from the memory a rooted sorrow,
Raze out the written troubles of the brain
And with some sweet oblivious antidote
Cleanse the stuff'd bosom of that perilous stuff
Which weighs upon the heart?
Doctor: Therein the patient
Must minister to himself.
*Macbeth: Throw physic to the dogs; I'll none of it.**

*William Shakespeare: Macbeth, V.iii. 40-47, c. 1606.

Laboratory Letter

Creatinine and Creatine Phosphokinase (CPK)

Why creatinine?

Because it's the best single serum test for evaluating renal function. And because, when measured with urine creatinine, it can be used to calculate creatinine clearance—the most commonly used test to approximate glomerular filtration rate.

The Council on the Kidney of the American Heart Association has established these criteria for evaluating severity of established renal disease:[1]

Class A
- Primary: Glomerular filtration rate normal
- Secondary: Serum creatinine normal

Class B
- Primary: Glomerular filtration rate reduced more than 50%
- Secondary: Serum creatinine normal to 2.4 mg/100 ml

Class C
- Primary: Glomerular filtration rate 10% to 50% of predicted normal
- Secondary: Serum creatinine, 2.5 to 4.9 mg./100 ml.

Class D
- Primary: Glomerular filtration rate 10% to 20% of predicted normal
- Secondary: Serum creatinine, 5.0 to 7.9 mg/100 ml

Class E
- Primary: Glomerular filtration rate less 10% of predicted normal
- Secondary: Serum creatinine, 8 to 12 mg/100 ml

Class F
- Primary: Glomerular filtration rate less than 5% of predicted normal
- Secondary: Serum creatinine greater than 12 mg/100 ml

BUN/Creatinine Ratio

Is there anything else you ought to know about creatinine and creatinine clearance?

There must be many things, but two spring immediately to mind: (1) If pre-renal azotemia exists (from reduced renal plasma flow due to dehydration, congestive failure, shock, or circulatory slowing in desperately sick patients), you ought to anticipate a discrepancy between BUN and creatinine. In most of these instances, the ratio of BUN to creatinine will exceed 10:1.[2] If true renal insufficiency exists, however, the ratio is usually less than 10:1. To summarize and elaborate:

(A) If BUN/creatinine ratio is more than 10:1, following more likely:
pre-renal azotemia from dehydration, shock, heart failure
excess protein intake when renal function is depressed
blood in bowel
tissue breakdown in starvation, fever, burns, steroid therapy, or any wasting pre-terminal state
urinary tract infection
occasionally hemorrhagic or embolic glomerulonephritis
ureterocolostomy

(B) If BUN/creatinine ratio is less than 10:1, following more likely:
renal insufficiency
low protein intake
repeated dialysis for chronic renal disease
severe diarrhea or vomiting in chronic renal disease
severe hepatic insufficiency with renal insufficiency

(2) The creatinine clearance depends on age.[3] As you age, you clear less creatinine through your kidneys. For this reason, creatinine clearance declines as you grow older.

Normal Range for Creatinine Clearance

Age	Men	Women
20-29	100-135	85-115
30-39	90-120	75-100
40-49	80-110	70- 90
50-59	75-100	65- 85
60-69	65- 90	55- 75
70-79	60- 80	50- 65
80-89	45- 60	35- 50
90-99	30- 45	25- 40

Now, CPK

Which brings us to creatine phosphokinase (CPK).

Why CPK at all? Aren't there enough enzyme tests already? Why complicate matters with yet another?

Because CPK isn't like the others.

You see, there isn't any CPK in the liver. It's in skeletal, smooth, and heart muscle. And in brain tissue. But not in the liver. Think about that just a moment. Alkaline phosphatase, LDH SGOT, and SGPT abound in the liver. But not CPK. So? So, if CPK is strikingly up, you can bet muscle damage—not liver damage—is the source. If on the other hand, the other enzymes are out of sight and CPK is normal, you can surmise the problem's inside Glisson's capsule.

Two Rumors, Three Bicycles

Recently I got the chance to chase down two rumors with three bicycles. The first rumor was that strenuous exercise elevated CPK. The second was that CPK broke down quickly after being placed in a serum vial. So, when three of our employees went on an 80 mile bicycle ride, we drew their blood when they returned and checked these same serum samples again after the sample sat on the counter at room temperature for three and five days. This is what was found:

Value After Three and Five Days

	Initial Value	at room temperature		Normal upper
Bicyclists	after ride	day three	day five	limits
Woman	65	70	65	50
Man	115	115	120	75
Man	160	160	155	75

As you can see, strenuous exercise elevated the CPK so it exceeded the upper limit by 15 to 85 units—confirming the first rumor. But CPK levels did not decline —even after sitting for five days—spiking the second rumor.

Relative CPK Magnitudes

Because muscle is so rich in CPK (The ratio of CPK activity in skeletal to heart muscle is 10:1[4]), almost anytime you cut, cauterize, bruise, stretch, manipulate or otherwise tamper with muscle, CPK will rise. Yes, that's true, say proponents of CPK use, ". . . but not significantly." So the question becomes: "What do you consider significant?" To try to answer that I've done some moseying around the literature with these results:

	Average increase of upper limit
Muscular dystrophy[5]	
Duchenne type	100 fold increase
Limb-Girdle	8 fold increase
Fascioscapulohumeral	3 fold increase
Myocardial Infarction[5-7]	10 to 40 fold increase
Major Surgery,[8] postoperative levels	
thoracic	8 fold increase
open heart	12 fold increase
intra-abdominal	9 fold increase
Urological Procedures with cutting of bladder muscle[9]	3 fold increase
IM Injection[10]	2-6 fold increase

Brain Damage and CPK

One of the odd things about CPK is that it consistently goes up in brain damage, yet on electrophoresis of CPK, the source of this elevated CPK appears to be muscle—not brain tissue.

From Australia comes word that CPK levels were elevated in all of 22 cases of encephalitis and meningitis.[11] And American psychiatrists report high CPKs in 24 of 37 acute psychotic patients.[12] But perhaps the best study comes from the British.[13] They report the following:

	Number of Patients	Number with Abnormal CPK	Number with Levels Greater than 10 normal	Number with Levels Greater than 20 times normal
Head Injuries	14	14	13	7
Strokes	21	15	2	0
Meningitis	7	3	0	1

To my knowledge, CPK is the only enzyme in the peripheral blood that goes up when a stroke occurs. This property could make CPK a valuable test in assessing brain damage or in differentiating between cerebrovascular insufficiency versus cerebrovascular necrosis.

Alcohol Ingestion and CPK

Yet another dilemma occurs in alcoholics. Although many alcoholics have liver damage, almost as many have muscle injury. In St. Louis, Perkoff, et al. observed a five-fold increase in CPK of 21 alcoholics compared to normal subjects.[14] And in Philadelphia, Lafair and Myerson reported these observations:[15]

	Number of Patients	Number with Abnormal CPK	Mean Peak Value of CPK
Chronic Alcoholics with no recent drinking	11	0	Normal
Chronic Alcoholics with acute muscle pain	6	6	4.4 times upper limit of normal
Chronic Alcoholics with delerium tremens	24	21	8.6 times upper limit of normal
Chronic Alcoholics admitted with acute intoxication	20	15	5.4 times upper limit of normal

Myocardial Infarction and CPK

Just a word about interpreting CPK in myocardial infarction. CPK acts essentially like a sensitive short-lived SGOT. CPK rises sooner than SGOT (three to six hours vs. six to 12 hours), peaks higher (40 times upper limit vs 12 times upper limit), and drops to normal quicker (perhaps a few hours). Here is some information indicating how CPK contrasts with SGOT and LDH.[16]

Post-Myocardial Infarction	Percent with Elevated Values		
	CPK	SGOT	LDH
1 day	100%	95%	87%
4 days	88%	96%	96%
7 days	50%	58%	70%
10 days	30%	50%	40%
14 days	0%	20%	40%

Hypothyroidism and CPK

Then there is the tricky business of elevated CPK levels in hypothyroidism (and of decreased CPKs in hyperthyroidism). No one knows why for sure, but hypothyroid patients run CPKs about eight times the normal mean, with levels reaching two to five times the upper limit.[17,18] Furthermore, the degree of CPK abnormality parallels the degree of hyperthyroidism.

A Final Note

I don't want to leave you with the impression I devote all of my energy digging in dark corners of the literature. Not so. I occasionally corroborate what I read, in light of local knowledge.

To check the validity of the BUN/Creatinine ration in distinguishing between pre-renal azotemia and true renal damage, I asked two colleagues, Doctors Patrick Ward and Desmond Burke, pathologists at Mt. Sinai in Minneapolis, to gather records on 25 patients with congestive failure—far and away the most common cause of pre-renal azotemia. I did so because the Mt. Sinai SMA—12/60 simultaneously measures BUN and creatinine on all patients.

In all of the congestive failure patients, the BUN/Creatinine ratio was greater than 10:1. In 22 of 25 patients, the ratio exceeded 11:1. The mean ratio was between 18:1 and 19:1.

And, with the help of Doctor David Kvistberg, biochemist at Lufkin Medical Laboratories, I checked out the magnitude of CPK elevations in chronic alcoholics and hypothyroidism. In 14 alcoholics admitted to an alcoholic treatment center, he found three with high CPKs. None of these CPKs surpassed 1.3 times the upper limit of normal. Among 13 patients with low T-4s (Murphy-Pattee), six had elevated CPKs. The highest value, 350 units or about five times the upper limit of normal for women, occurred in a patient with a T-4 of 0.1.

Richard L. Reece, M.D.
Minneapolis, Minnesota

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See Clinical Considerations section which follows...

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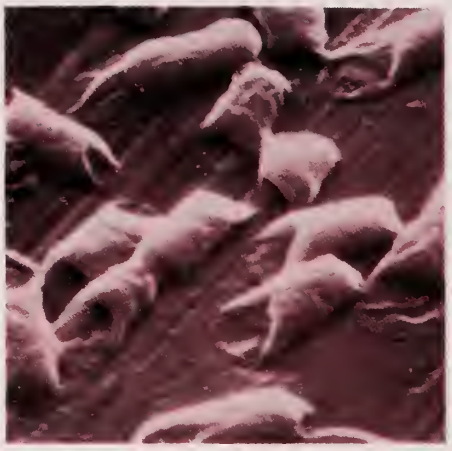
*In suspected or documented gram-negative sepsis due to susceptible organisms, GARAMYCIN Injectable may be considered as initial therapy. Th decision to continue therapy with this drug should be based on the results o susceptibility tests, the severity of the infection, and the important concept contained in the Warning Box below.

An indispensable spectrum for today[1-3]

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Proven clinical efficacy[1,4-13]

GARAMYCIN Injectable may be lifesaving in septicemia... may give a dramatic response in wounds and burns complicated by sepsis. GARAMYCIN Injectable has also demonstrated outstanding results in serious gram-negative infections other than sepsis, such as serious respiratory infections and selected urinary tract infections. To date, GARAMYCIN Injectable has been the subject of more than 1,500 published papers and 12 international symposia.





Note: The photomicrographs of gram-negative organisms reproduced here were obtained by a relatively new process employing a scanning beam electron microscope. The pathogens represented are *Klebsiella pneumoniae*, *Escherichia coli*, and *Proteus mirabilis*. The colors shown here are an artist's representation. The magnification is 10,000X.



WARNING: Patients treated witl GARAMYCIN Injectable should be under close clinical observation because the potential toxicity associated with the use of this drug.

Ototoxicity, both vestibular and auditory, can occur in patients, pa and those with pre-existing renal dam e, treated with GARAMYCIN Injectab usually for longer periods or with gh doses than recommended.

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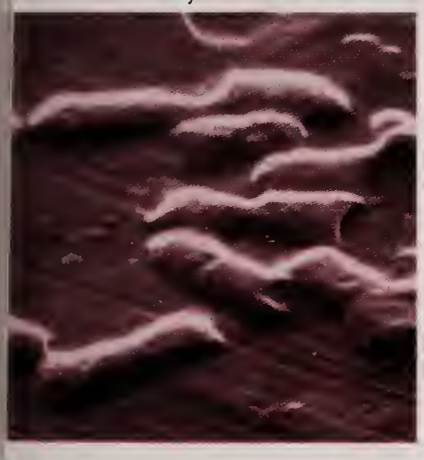
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A high degree of sensitivity maintained[14-16]

Bacterial resistance to GARAMYCIN Injectable has not been a problem to date. In the laboratory, resistance has been demonstrated to develop slowly in stepwise fashion. No one-step mutations to high resistance have been reported. One investigator noted: "In the experience so far with [gentamicin], which is 7 or 8 years, in centers where it's been restricted to parenteral use, resistance has not appreciably changed."[14] Another authority "...found very little emergence of resistance" during eight years of use.[15]

In a survey of published studies on resistance to gentamicin, Weinstein and co-workers[16] report little change in bacterial sensitivity since 1963 in the percentage of sensitive strains. *In vitro* sensitivity was determined in all cases by the tube-dilution method.



Relatively low incidence of adverse reactions[3,14,17]

As with certain other aminoglycoside antibiotics, ototoxicity (primarily vestibular with gentamicin) and potential nephrotoxicity are risks of therapy.

Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy.

In contrast to kanamycin, neomycin, and streptomycin, which primarily cause deafness or difficulties in the auditory end organs of the eighth nerve, gentamicin primarily causes labyrinthian dysfunction.[14] This dysfunction, manifested by dizziness (not deafness) has, in most cases, been transitory.

As to nephrotoxicity, according to Finland,[3] "as in the case of kanamycin, the nephrotoxicity was found to be largely 'potential,' and very little if any has been encountered except with obviously excessive doses or in patients with already damaged kidneys."

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ephrotoxic, and this should be kept in ind when it is used in patients with re-existing renal impairment.

Monitoring of renal and eighth nerve nction is recommended during therapy f patients with known impairment of nal function. This testing is also commended in patients with normal nal function at onset of therapy who evelop evidence of nitrogen retention ncreasing BUN, NPN, creatinine or liguria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

Usage in Pregnancy: Safety for use in pregnancy has not been established.

See Clinical Considerations section which follows...

When preculture signs point to gram-negative sepsis...

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WARNING: Patients treated with GARAMYCIN Injectable should be under close clinical observation because of the potential toxicity associated with the use of this drug.

Ototoxicity, both vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment.

Monitoring of renal and eighth nerve function is recommended during therapy of patients with known impairment of renal function. This testing is also recommended in patients with normal renal function at onset of therapy who develop evidence of nitrogen retention (increasing BUN, NPN, creatinine or oliguria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause toxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

USAGE IN PREGNANCY Safety for use in pregnancy has not been established.

INDICATIONS GARAMYCIN Injectable is indicated, with due regard for relative toxicity of antibiotics, in the treatment of serious infections caused by susceptible strains of the following microorganisms:

Pseudomonas aeruginosa, Proteus species (indole-positive and indole-negative), **Escherichia coli** and **Klebsiella-Enterobacter-Serratia** species.

Clinical studies have shown GARAMYCIN Injectable to be effective in septicemia and serious infections of the central nervous system (meningitis), urinary tract, respiratory tract, gastrointestinal tract, skin and soft tissue (including burns).

Bacteriologic tests to determine the causative organisms and their susceptibility to gentamicin should be performed.

Bacterial resistance to gentamicin develops slowly in stepwise fashion; there have been no one-step mutations to high resistance.

In suspected or documented gram-negative sepsis, GARAMYCIN may be considered as initial therapy. The decision to continue therapy with this drug should be based on the results of susceptibility tests, the severity of the infection, and the important additional concepts contained in the "Warning Box." In the neonate with suspected sepsis or staphylococcal pneumonia, a penicillin type drug is usually indicated as concomitant antimicrobial therapy.

GARAMYCIN Injectable has been shown to be effective in serious staphylococcal infections. It may be considered in those infections when penicillins or other less potentially toxic drugs are contraindicated and bacterial susceptibility testing and clinical judgment indicate its use.

CONTRAINDICATIONS A history of hypersensitivity to gentamicin is a contraindication to its use.

WARNINGS (See "Warning Box.")

PRECAUTIONS Neuromuscular blockade and respiratory paralysis have been reported in the cat receiving high doses (40 mg./kg.) of gentamicin. The possibility of these phenomena occurring in man should be considered if gentamicin is administered to patients receiving neuromuscular blocking agents such as succinylcholine and tubocurarine.

Treatment with gentamicin may result in overgrowth of nonsusceptible organisms. If this occurs, appropriate therapy is indicated.

ADVERSE REACTIONS

Nephrotoxicity: Adverse renal effects, as demonstrated by rising BUN, NPN, serum creatinine and oliguria, have been reported. They occur more frequently in patients with a history of renal impairment treated with larger than recommended dosage.

Neurotoxicity: Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss.

Numbness, skin tingling, muscle twitching, and convulsions have also been reported.

Note: The risk of toxic reactions is low in patients with normal renal function who do not receive GARAMYCIN Injectable at higher doses or for longer periods of time than recommended.

Other reported adverse reactions, possibly related to gentamicin, include increased serum transaminase (SGOT, SGPT), increased serum bilirubin, transient hepatomegaly, decreased serum calcium; splenomegaly, anemia, increased and decreased reticulocyte counts, granulocytopenia, thrombocytopenia, purpura; fever, rash, itching, urticaria, generalized burning, joint pain, laryngeal edema; nausea, vomiting, headache, increased salivation, lethargy and decreased appetite, weight loss, pulmonary fibrosis, hypotension and hypertension.

DOSAGE AND ADMINISTRATION GARAMYCIN Injectable may be given intramuscularly or intravenously.

For Intramuscular Administration:

PATIENTS WITH NORMAL RENAL FUNCTION*

Adults: The recommended dosage for GARAMYCIN Injectable for patients with serious infections and normal renal function is 3 mg./kg./day, administered in three equal doses every 8 hours.

For patients weighing over 60 kg. (132 lb.), the usual dosage is 80 mg. (2 cc.) three times daily. For patients weighing 60 kg. (132 lb.) or less, the usual dose is 60 mg. (1.5 cc.) three times daily.

In patients with life-threatening infections, dosages up to 5 mg./kg./day may be administered in three or four equal doses. This dosage should be reduced to 3 mg./kg./day as soon as clinically indicated.

*In children and infants, the newborn, and patients with impaired renal function, dosage must be adjusted in accordance with instructions set forth in the Package Insert.

For Intravenous Administration:

The intravenous administration of GARAMYCIN Injectable is recommended in those circumstances when the intramuscular route is not feasible (e.g., patients in shock, with hematologic disorders, with severe burns or with reduced muscle mass).

For intravenous administration, in adults, a single dose of GARAMYCIN Injectable may be diluted in 100 or 200 cc. of sterile normal saline or a sterile solution of dextrose 5% in water; in infants and children, the volume of diluent should be less. The concentration of gentamicin in solution, in both instances should normally not exceed 1 mg./cc. (0.1%). The solution is infused over a period of 1 to 2 hours.

The recommended dose for intravenous administration is identical to that recommended for intramuscular use.

GARAMYCIN Injectable should not be physically pre-mixed with other drugs, but should be administered separately in accordance with the recommended route of administration and dosage schedule.

HOW SUPPLIED GARAMYCIN Injectable, 40 mg. per cc., 2 cc. multiple dose vials for parenteral administration.

Also available, GARAMYCIN Pediatric Injectable, 10 mg. per cc., 2 cc. multiple-dose vials for parenteral administration.

APRIL, 19

AHFS Category 8:12.

For more complete prescribing details, consult Package Insert or Physicians' Desk Reference. Schering literature is also available from your Schering Representative or Professional Services Department, Schering Corporation, Kenilworth, New Jersey 07033.

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Review—

Psychiatric Disabilities of the Vietnam Veteran

Review and Implications for Treatment

GAYLE K. LUMRY, Ph.D., CHERRY B. CEDARLEAF, M.D.
M. SUZANNE WRIGHT, Ph.D., AND GORDON A. BRAATZ, Ph.D.

APPROXIMATELY ONE-FOURTH of all hospitalized Vietnam veterans are treated for a primary psychiatric disability. Psychological factors also enter into physical illnesses and the magnitude of this problem is such that more information is needed in order to formulate treatment objectives.

Method

The clinical records of 458 psychiatric and 48 medical patients were reviewed. The psychiatric sample included patients under 26 years of age, admitted to the psychiatric service of the Minneapolis Veterans Hospital from 1963 to 1969, and who were otherwise free of serious medical problems. The 48 medical controls, who were also under 26 years of age, represented a wide variety of medical disabilities and were seen at the Minneapolis Veterans Hospital from 1963 to 1969. The only difference between the two groups in respect to military experience was that about one-third of the psychiatric patients were still on active duty at the time of the admission and none of the medical patients were on active duty.

Results

Demographic Characteristics

One-fourth of the psychiatric sample did not complete high school. Most of the veterans had little or no pre-service work or technical training. Of the psychiatric patients, 60% were single and the married veterans almost uniformly reported marital problems sufficient to require counselling. Also 40% of the psychiatric patients were from homes which were broken by divorce, separation or desertion, and in 48% of the families there was a severe degree of psychopathology including alcoholism, child-abuse, and psychotic episodes in one or both parents.

Diagnoses

The clinical diagnoses are shown in Table 1. To a far greater extent than is true of older patients there were ambiguities in diagnoses since physicians found it necessary to employ a long series of modifying phrases even to approximate a gross description of a patient. As noted by Siegel,[2] at one end of the spectrum are the patients with a character disorder who are relatively well integrated and who relate well socially. At the other end of the spectrum are severely withdrawn, psychotic (usually schizophrenic) individuals who have great difficulty with interpersonal relationships and socialization. Between these two groups are the patients who vary in ability to relate to others and in the degree of withdrawal.

Adjustment Deficiencies

A sample of 200 patients was evaluated for deficiencies in six major life areas. As can be seen from Table 2, the marked vocational and interpersonal maladjustment (especially failure in marital adjustment) is striking. The magnitude of these difficulties is even clearer when it is recognized that three-fourths of the psychiatric group had

TABLE 1
Diagnostic Categories* of Psychiatric Patients Under 26 Years of Age, Minneapolis VA Hospital

	Total	Percent
Schizophrenia	153	33.4%
Paranoid	60	
Chr. Undiff.	51	
Other	42	
Affective disorders	3	0.7%
Personality disorder	166	36.2%
Sociopathic personality	73	
Personality trait disturbance	44	
Personality pattern disturbance	31	
Other	18	
Psychoneurotic disorders	110	24.0%
Depressive neurosis	41	
Anxiety neurosis	47	
Other	22	
Other diagnoses	26	5.7%
Total	458	

*Diagnostic nomenclature (DSM-I) used for comparison purposes.

Read at the Fifteenth Annual Conference, Veterans Administration Cooperative Studies in Psychiatry, Houston, Texas, April 4, 1970

From the Psychology and Psychiatry Services, Veterans Administration Hospital, Minneapolis.

Reprint requests to Veterans Administration Hospital, 54th Street and 48th Avenue South, Minneapolis, Minnesota 55417.

difficulties in at least three of the six areas of life adjustment.

TABLE 2
Percentage of Patients Having Deficiencies in Six Life Adjustment Areas

Life Adjustment Areas	Percent Deficient
Education: School attainment below intellectual potential. Lacks vocational training or employable skills	52%
Vocation: Not well established in a vocation	84%
Socialization: Does not have satisfying interests or hobbies	55%
Sexual Adjustment: Expresses conflict about sex	58%
Interpersonal Adjustment: Unable to maintain satisfying interpersonal relationships	76%
Family Relationships: Still very dependent upon family, considerable conflict with family	57%

Acting Out Potential

Another important consideration in evaluation of treatment needs is the assessment of behavior which might indicate "acting out potential." These proclivities directed outwardly in anti-social acts and assaultive behavior or self-inflicted injuries, drug addiction or alcohol abuse, must be considered in treatment planning.

TABLE 3
"Acting-Out Potential" of Young Veteran Patients (N=458)

	Active Service N-157	Other Veterans N-301	Vietnam Veterans N-85	Total # N-458
Alcohol Problems	42.0%	40.0%	51.7%	40.8%
Drugs	25.4	11.8	16.4	16.5
Suicidal or Assaultive	63.6	36.8	43.5	54.1
Suicidal Acts	35.6	15.9	21.1	26.6
Disciplinary Problems, Civilian or Military	24.1	26.2	27.0	25.7

Comparison of the MMPI Profiles

The mean MMPI profile for the medical school sample reflects considerably less distress than the psychiatric sample. This is even more interesting in view of the fact that two-thirds of the medical control group had served in Vietnam while only 18% of the psychiatric group had served there. The mean profiles of the psychiatrically disabled veterans who have had active duty in Vietnam could not be reliably discriminated from those who had served elsewhere, or from those who were in active service at the time of the psychiatric hospitalization.

TABLE 4
Mean MMPI T Scores for the Vietnam Era Patient Samples

	Psychiatric Patients	Medical Patients
Lie Scale (L)	48.4	47.9
Validity Scale (F)	72.8	60.4
Correction Scale (K)	49.3	54.2
Hypochondriasis (Hs)	65.6	62.3
Depression (D)	76.5	62.3
Hysteria (Hy)	68.7	62.7
Psychopathic Deviate (Pd)	76.3	64.5
Masculinity-Femininity (Mf)	63.8	56.3
Paranoia (Pa)	70.6	56.4
Psychasthenia (Pt)	77.7	63.3
Schizophrenia (Sc)	82.7	67.8
Hypomania (Ma)	67.8	62.5
Social Introversion (Si)	59.4	51.9

Conclusions

This study suggests that the psychiatric disabilities of Vietnam veterans follow a continuous pattern like those found in civilian practice. In addition, almost all the psychiatrically disabled veterans have had education, vocational or social problems of a serious nature prior to entering active duty. Sexual adjustment has not been adequate and general, interpersonal adjustment and family relationships can be characterized as either unsatisfactory or insufficient. From our data it would appear that active military duty may exacerbate symptoms, but is not a sufficient cause in itself to explain their disabilities and psychiatric illnesses. Moreover duty in Vietnam in itself cannot be blamed for the psychiatric disabilities of these individuals. Indeed, most of our psychiatrically disabled veterans have not served in the combat area.

Recommendation for Treatment

A full range of psychiatric facilities could effectively meet the needs of these young patients. A patient's involvement in such a multifaceted treatment program should begin with a thorough evaluation in an in-patient service for a period of time sufficient for the formulation of an effective, long-term program. Major areas of personality adjustment must be approached, especially those areas which were deficient prior to the veteran entering the Armed Forces. Most of our patients could be treated on some form of psychiatric service which does not require full-time in-patient care. Married patients and single patients with close parental family ties might find a modification of the day hospital most effective. The Minneapolis Vet-

rans Hospital has already achieved considerable uccess with these individuals. Some individuals /ho do not fit this category may require some orm of community living arrangement. Many pa-ients need to take steps in order to achieve inde-endence from their parents and to acquire suffi-ient integration to maintain themselves without upport in the greater society. Perhaps such a pro-ram could involve an apartment complex housing 6-24 residents which could provide the varying legrees of independence and yet, enhance "in a rotective setting" social integration. Certainly, educational-vocational programs could be pursued luring the day with evening activities directed owards socialization and improved interpersonal elationships. Group therapy, discussion of topics f general interest and concern, social activities nd recreation could be included. In addition to a rofessional staff, hopefully, volunteers would also be available to provide the necessary peer relationships as well as some of the adult leadership required.

Summary

It is evident that varied programs are needed for Vietnam veterans and these must be different from the usual medical models we have used in the past. Most of our patients have not developed stability and maturity before entering the Armed Forces and it is essential for them to have assistance in developing these characteristics if they are to cope with society and avoid recurrent hospitalization. Immeasurable benefits are to be gained by helping these patients to achieve greater productivity and a happier, more comfortable relationship in our society. To create and implement such a program requires a more flexible approach than orthodox, in-patient psychiatric care.

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Cerebral Concussion Syndrome in Children

Schnitker described a syndrome of concussion in 11 children who suffered minor head injury. The clinical picture followed a blow to the frontal or temporal skull, after which there was a lucid interval with crying, vomiting, and mild shock. These symptoms were followed by a period of traumatic stupor that closely resembled the classic syndrome of extradural hematoma in the adult.

According to Schnitker, the cause was probably a mild, localized, cerebral edema extending to the region of the diencephalon. The condition should be differentiated from that of cerebral contusion in which the injury is more severe and there is prolonged unconsciousness. Recovery was complete in 24 hours.

Durham, Robert H.—Encyclopedia of Medical Syndrome
Hoeber Medical Division, Harper and Row, New York

Psychiatry

The Schizophrenic

The Pill or Not the Pill—Fluphenazine Enanthate an Answer

WILLIAM W. BRAUER, M.D.

THE AUTISTIC meandering of a schizophrenic reverie leaves little room for logic. The daily repetitious question of "Should I take my pill?" is a logical one, for without medications the schizophrenic may have a 75 percent chance of rehospitalization.[1] Taking a pill involves timing, trust, memory, and consistency. Unfortunately, schizophrenic disorganization disrupts these traits.

Until recently physicians had to rely on either the patient, the relatives, or the nurse to ensure that medication was taken properly by the schizophrenic patient.

Introduction

Fluphenazine hydrochloride[2,3] (Prolixin) is known to be an effective antipsychotic drug. It is fat-soluble and released slowly from fatty tissue. Esterification with various acid esters, particularly Enanthic acid, further reduces the rate of release of Fluphenazine in the body. Dissolving this ester in sesame oil constitutes the injectable Fluphenazine Enanthate.

This depot Fluphenazine product is released from the buttock injection site and the sustained therapeutic effect may continue for two weeks after the injection. Side effects are similar to those of the oral Fluphenazine and caution is necessary, as once the drug is injected it cannot be retrieved. Used properly, however, Fluphenazine Enanthate affords numerous therapeutic advantages.

Indications

The Acutely Psychotic

An acutely psychotic and delusional schizophrenic is often too disturbed to accept pills. He thinks that medication destroys his grandiose talents or that it may indicate a poison plot.

A 20-year-old disturbed schizophrenic was admitted to the hospital forcefully after several nights of wandering aimlessly throughout the city. Medication was refused because it would "disrupt my religious powers." After he received ½ cc (12½ mg) of Fluphenazine Enanthate, his threats to leave the hospital were discussed for the next few days. Rather rapidly his philosophical and religious musings decreased and he cooperated in accepting treatment. Five days after the initial injection, a repeat injection was given and benztropine mesylate (Cogentin), one mg tablet twice a day, was added to the therapy. Within several weeks this young man was discharged from the hospital and has remained on a weekly dosage of 12½ mg of Fluphenazine Enanthate. He has worked steadily the past six months and faithfully continues his medication.

Merry-go-round Syndrome

Many schizophrenics demonstrate "the merry-go-round syndrome;"[4] repetitive hospitalizations precipitated by interruption of phenothiazine therapy by the patient. His improvement on phenothiazine therapy allows a false feeling of recovery and, either because of this or other rationalizations, he discontinues the medication.

A 26-year-old man had a six-year history of schizophrenia. Following an acute psychotic episode in college, treatment has included electroshock therapy, medications, and approximately 10 re-hospitalizations. During my two-year care of this young man, he has been re-hospitalized on three occasions, each time within two to four weeks of his unilaterally discontinuing his phenothiazines. Despite periodic review of these failures, he gained no insight. On his last hospitalization Fluphenazine Enanthate therapy was begun: weekly injections of ½ cc (12½ mg). He has worked now a total of four months, a feat impossible in the preceding six years. He has remained now with his parents, although on five previous occasions in the past six years he had eloped and ended up being hospitalized in such distance places as California, New York, and Canada. Even now he continues to lack insight and may admit that he has stopped chlorpromazine (Thorazine) or other additional medications he receives. On occasion he has marked dystonia and extrapyramidal side effects; at those times he admits discontinuing his Cogentin. Recently, however, he has taken the Cogentin faithfully and appears to be learning the necessity for medication.

Periodic Aggression

The schizophrenic with periodic aggression represents a dangerous threat to the community. A homicidal, paranoid patient who has recovered from a psychosis through pharmacotherapy will usually stay well as long as he remains on medica-

Reprint request address to: Dr. W. W. Brauer, 527 Medical Arts Building, Minneapolis, Minnesota 55402.

tion. The psychiatrist in this situation has a duty to insure that this potentially aggressive individual is on medication and thus well under control.

A 19-year-old man had been treated with a five-month hospitalization one year prior to my care. In the past year and one-half, he has had aggressive outbursts at home in which he attacked his father or mother. At various times they received trauma sufficient for them to be hospitalized. When medication including Thorazine and oral Fluphenazine was insufficient to prevent his outbursts, he began Fluphenazine Enanthate weekly injections of ½ cc (12½ mg). In the past seven months he has remained at home, rather isolated from peers and the community, but has had no aggressive nor violent outbursts. He is cooperative with his parents and also with his weekly hospital visits for his medication. He speaks only rarely of his delusional system which in the past consisted of thoughts that people were looking at him, talking about him, and thinking him homosexual. He no longer mentions the delusions that other people are accusing him of molesting young women.

Discussion

The three problem patients above are responding well to treatment. The main feature of their treatment includes Fluphenazine Enanthate, although simultaneously all received mega-vitamin treatment as advocated by Hoffer.[5] Other adjuncts included daily Cogentin to control the extrapyramidal effects and occasional simultaneous use of oral phenothiazines. Although no proof exists that Fluphenazine Enanthate is the sole agent responsible for their improvement, care of these patients would have been markedly handicapped or would have failed without the use of intramuscular, long-acting, antipsychotic medication.

Advantage of Injectable

Cole[3] points out two possible advantages of the injectable over the oral form of Fluphenazine. One is that the drug is absorbed into the blood stream and goes through the lungs *to the brain before passing through the liver*. It may well be that chronic schizophrenic patients with long histories of exposure to phenothiazines have developed hepatic enzymes. These enzymes are highly efficient at metabolizing and deactivating orally administered phenothiazine medication. The use of the long-acting injectable form may provide an effective level of drug in the brain which may have been achievable only by extraordinarily high oral doses of similar medications. The second advantage is that the long-acting injectable Fluphenazine is more effective because it provides to all patients a *higher level of drug in the central nervous system* than would be achieved by much higher doses of oral Fluphenazine.

Many clinicians report using Fluphenazine Enanthate at fortnightly intervals (every two weeks) and may give one cc (25 mg) or higher doses per injection. Yet many patients complain bitterly of extrapyramidal side-effects and listlessness the second through the fourth day of post-injection therapy. To decrease this reaction, weekly shots at a decreased dosage as illustrated in the examples decrease the side-effects of the medication; however, the more frequent injections decrease the advantage of the long-lasting effect of the medication. Extrapyramidal effects are fairly well controlled through the use of such drugs as Cogentin. Studies indicate that the long-acting extrapyramidal side-effects are no different from those of routine anti-psychotic drugs although the onset may be different and the dystonic reactions a little more bizarre.[3] Hematologic and liver disturbances are rare, but periodic blood tests are advisable.

Advantage to Side Effects

An interesting advantage acrues from the side-effects of the medication. Extrapyramidal effects are disturbing to the patient and point out the necessity vividly described in the patient with the merry-go-round syndrome for medication to counteract the muscular discomfort. From a behavioral modification standpoint, patients on depot Fluphenazine eventually learn that medication is important. While they may neglect taking phenothiazines because "it doesn't do me any good," they will happily and conscientiously take the anti-parkinsonism agents to relieve physical discomfort. This patterned performance is helpful in learning medication schedules and proves useful if at a future time medication is shifted to oral Fluphenazine or other phenothiazines. "The pill or not the pill" becomes a forgotten issue in many of these improved schizophrenic patients.

Summary

The long-acting injectable form of Fluphenazine has unique value in the treatment of schizophrenia. It is indicated for use in patients who refuse oral medications, patients with exacerbations of illness due to discontinuation of medication, and individuals with severe paranoid homicidal tendencies who are potentially a threat to the community. Fluphenazine Enanthate appears more active in causing extrapyramidal and lethargic effects than has been reported elsewhere. Titra-

tion of medication and use of antiparkinsonism drugs may be necessary. Fluphenazine Enanthate is the drug of choice in some schizophrenic illnesses and merits wider popular use by the medical profession.

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5. Hoffer A: A Program for Treating Schizophrenic and Other Conditions Using Megavitamin Therapy. Modern Press, Saskatoon, Canada. 1965.

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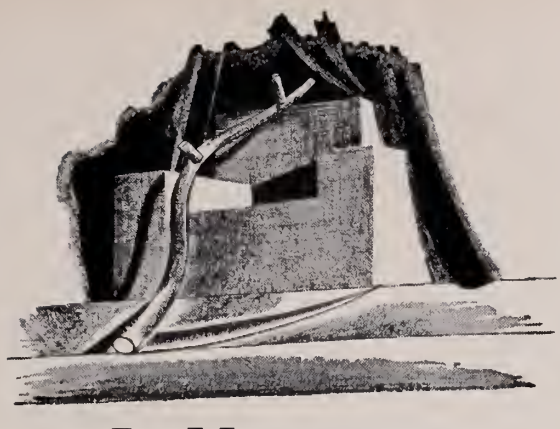
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In Memoriam

God's finger touched him, and he slept.—Tennyson

OMER E. SNYKER, M.D.

Dr. Omer E. Snyker, 66, Ely physician, died September 2. Born in St. Paul, Dr. Snyker took pre-medical courses at the University of Minnesota in the early 1920s and later studied part-time at Loyola University Medical School, getting his degree there in 1934. Four years later he chose Ely to set up his practice. In 1945 he converted the brick school into Ely's first hospital.

He was a member of the Range Medical Society and the American Medical Association and was an Associate Member of the Minnesota State Medical Association.

Dr. Snyker is survived by his sons, Donald, Gary and Kenneth, and one daughter, Mrs. William Mackie.

CHARLES W. FROATS, M.D.

Dr. Charles W. Froats, 72, a former chief of the medical staff of St. Luke's in St. Paul died August 30. His medical education was obtained at Northwestern University Medical School in Chicago.

He was a member of the Ramsey County Medical Society and the American Medical Association, a Fellow of the American College of Surgeons and the Central Association of Obstetricians and Gynecologists, a charter member of the Minnesota Society of Obstetrics and Gynecology, and a Life Member of the Minnesota State Medical Association.

Dr. Froats is survived by his wife, Doris, a daughter, Mrs. Thom Jordan and sons David J. and Charles W., Jr.

IVAN C, DIMMICK, JR,, M.D.

Dr. Ivan C. Dimmick, the senior staff physician at the Brainerd State Hospital, died July 25. He was 62. Dr. Dimmick came to the State Hospital in March of 1970 after retiring from military service with the rank of colonel.

He was a member of the Upper Mississippi Medical Society, the American Medical Association and the Minnesota State Medical Association.

Dr. Dimmick is survived by his wife, Marion.

EDWARD N. COOK, M.D.

Dr. Edward N. Cook, 66, Mayo Clinic urologist emeritus, died July 26. He was a member of the department of urology at the Mayo Clinic and professor of urology in the Mayo Graduate School of Medicine from 1936 until his retirement in 1970.

Born in St. Paul, Dr. Cook obtained his doctor of medicine degree from the University of Minnesota. He went to Rochester in 1930 as a fellow in surgery in the Mayo Graduate School.

Dr. Cook was certified as a specialist in urology by the American Board of Urology and was a member of the International Society of Surgery, the American Medical Association, the American Urological Association, the Southern Minnesota Medical Association, the North Central Section of the American Urological Association, the Zumbro Valley Medical Society, an honorary member of the Mexican Urologic Society and of the South Central Section of the American Urological Association. He was a Residency Member of the Minnesota State Medical Association.

Dr. Cook is survived by his wife, Jean, a son Edward and two daughters, Mrs. Carroll Berndt and Mrs. Bruce Nelson.

FREDOLPH H. MAGNEY, M.D.

Dr. Fredolph H. Magney, 86, Duluth physician, died September 6. Born in Ellsworth, Wisconsin, Dr. Magney graduated from the University of Minnesota Medical School in 1915 and established his practice in Duluth the following year.

He was a member of the American Medical Association, St. Louis County Medical Society and the state board of medical examiners. He was a fellow of the American College of Surgeons and had been chief of staff of all three Duluth hospitals. In 1955 he was given the Distinguished Service Award by the Minnesota State Medical Association and was a 50 Club and Life Member of this organization. A member of the St. Louis County Tuberculosis and Health Association, Dr. Magney was instrumental in that organization's acquisition of the first mobile tuberculosis detection unit.

Dr. Magney is survived by his wife, Ruth, and four sons, Roy, Robert, Paul, and Mark.

RAYMOND D. J. ALBRECHT, M.D.

Dr. Raymond J. Albrecht, 40, St. Paul specialist in obstetric and gynecology, died September 23. He was born in St. Paul and lived there all his life. Dr. Albrecht pioneered natural childbirth at St. Joseph's Hospital in St. Paul, and was on the staff of this hospital in addition to being a clinical professor of obstetrics and gynecology at the University of Minnesota.

He was a member of the Ramsey County Medical Society, a diplomat of the American Board of Obstetrics and Gynecology, a member of the American Medical Association and the Minnesota State Medical Association.

Dr. Albrecht is survived by his wife, Judith and four children, Lisa, Katherine, Mary and Paul.

HENRY D. DIESSNER, M.D.

Dr. Henry D. Diessner, 86, Minneapolis urologist, died September 21. He attended the University of Minnesota Pre-med School and graduated from Hahnemann Medical College in Philadelphia in 1909.

A former chief of staff of St. Barnabas Hospital, Dr. Diessner was a member of the Twin Cities Urological Society, the North Branch of the American Urological Society, the American Medical Association and the Hennepin County Medical Society. He was a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Diessner is survived by his wife, Eleanor, daughters Sylvia, Viola, Gladys and Laura. Dr. William Diessner of Waconia is his brother.

FRANK E. ELLISON, M.D.

Dr. Frank E. Ellison, 88, of Monticello died September 19. He participated actively in the civic life of Monticello and had been a member of the school board for 30 years, serving as its president for 27 years. In 1959, the high school awarded him a special award as the outstanding citizen in Monticello. In 1954 he was among a select group of citizens who were given a citation by Hamline University "for achievements and service in medicine and church leadership."

Educated at Hahnemann Medical School in Chicago, he was a member of the American Medical Association and the Wright County Medical Society and a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his wife, Caroline, and sons, John and Everett.

WILLIAM B. EILERS, M.D.

Dr. William Benit Eilers, 36, died September 7. He was born in Brooklyn, Iowa and attended Fairmont and Redwood Falls schools, graduating from the University of Minnesota Medical School in 1960.

After his discharge from the army, Dr. Eilers joined Cairns Clinic in Redwood Falls in 1963. He was a member of the MidMinnesota County Medical Society and the American Medical Association and a Residency Member of the Minnesota State Medical Association.

Dr. Eilers is survived by his wife, Marilyn, and children, Lynda, Kathryn, William, Kristin, Timothy and Patricia.

MANLEY F. JUERGENS, M.D.

Dr. Manley F. Juergens, 50, Stillwater physician, died September 5. He was reared in Belle Plaine, Minnesota, and graduated from the University of Minnesota Medical School in 1945. He served in the Army Air Force and practiced medicine in Minneapolis and Thief River Falls before moving to Stillwater in 1949 where he became a partner in the Stillwater Clinic.

He was a member of the Minnesota State Medical Association, Wakota County Medical Society, American Academy of Family Practitioners, Minnesota Academy of Family Practice, American Medical Association, Minnesota Heart Assocation, and the Lakeview Hospital Medical Staff of which he was a former chief of staff.

Dr. Juergens is survived by his wife, Harriet, and three sons, Hugh, Steven and Mark. Dr. H. M. Juergens of Belle Plaine is his father and Dr. John L. Juergens of the Mayo Clinic, Rochester, his brother.

CHARLES F. REICHELDERFER, M.D.

Dr. Charles Reichelderfer, Staples physician and surgeon for many years, died July 17. He was 70 years of age. He received his medical education at Northwestern University Medical School in Chicago, and after interning, moved to Staples where he opened his medical office in 1927 where he continued his medical practice until his death.

He was known in Staples as the "Father of the Vocational School" being one of the first to recognize the need for vocational training. He served as chief of staff at the Staples Municipal Hospital, as Health Officer and Registrar of Vital Statistics for many years, and was a member of the American Medical Association and the Upper Mississippi Medical Society and a Life Member of the Minnesota State Medical Association.

Dr. Reichelderfer is survived by his wife, Lylla, two daughters, Elaine and Cynnthia, and one son, Dr. Charles F. Reichelderfer, Jr. of Hyattsville, Maryland.

RICHARD E. ANDERSON, M.D.

Dr. Richard E. Anderson, Willmar physician, died August 26. He was 88 years of age. He went to Willmar in 1921 from Chicago where he had been engaged as a medical doctor for an insurance firm, and practiced there until 1951. The next two years he resided in Rock Island, Illinois, before returning to Willmar to continue his practice until his retirement in 1963.

Born in Rock Island, Illinois and graduating from the University of Illinois Medical School, Dr. Anderson interned at the County Hospital in Chicago.

He was a member of the American Medical Association and the Mid Minnesota Medical Society and a 50 Club and Life Member of the Minnesota State Medical Association. He is also a 50-year member of the Masonic Order and a past master of the Sharon Lodge, A.F.&A.M.

Dr. Anderson is survived by his wife, Caroline.

NORMAN H. BAKER, M.D.

Dr. Norman H. Baker, 67, Fergus Falls physician and surgeon, died September 23, on a hunting trip near Baudette, Minnesota. Educated at the University of Minnesota Medical School, Dr. Baker spent his entire private medical career in Fergus Falls.

He was a member of the American Medical Association, the Minnesota State Medical Association and the Park Region District and County Medical Society.

Dr. Baker is survived by his wife, Dr. Jeanette Baker, two sons, Dr. Richard Baker and Dr. Norman Baker, and a daughter, Dr. Jean Trousdale.

Iron therapy for anemia is almost as old as history itself



Celsus's empirical use of iron

Aulus Cornelius Celsus recommended an unusual form of iron therapy for the treatment of enlarged spleens—the oral administration of water that blacksmiths had used for dousing white-hot iron.

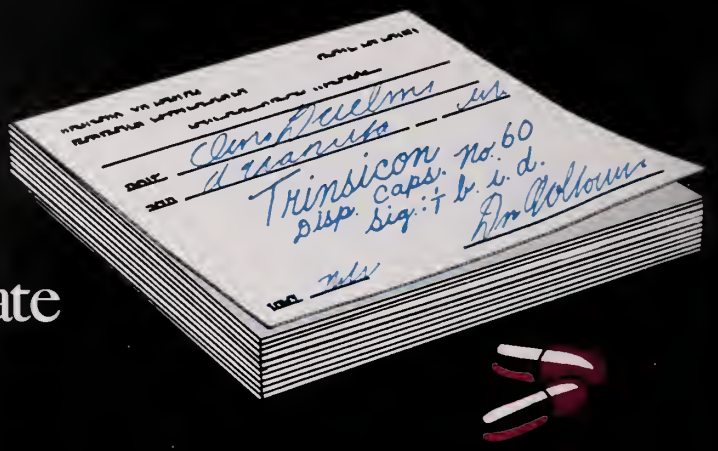
For more modern anemia therapy

Trinsicon®

Hematinic Concentrate with Intrinsic Factor

(See reverse side for prescribing information.)

Trinsicon®
Hematinic Concentrate with Intrinsic Factor



Description: Each Pulvule® contains—

Special Liver-Stomach Concentrate, Lilly (containing Intrinsic Factor)	240 mg.
Cobalamin Concentrate, N.F., equivalent to Cobalamin	7.5 mcg.

(The total vitamin B_{12} activity in the Special Liver-Stomach Concentrate, Lilly, and the Cobalamin Concentrate, N.F., is 15 micrograms.)

Iron, Elemental (as Ferrous Fumarate)	110 mg.
Ascorbic Acid (Vitamin C)	75 mg.
Folic Acid	0.5 mg.

Indications: Trinsicon is a multifactor preparation effective in the treatment of anemias that respond to oral hematinics, including pernicious anemia and other megaloblastic anemias and also iron-deficiency anemia. Therapeutic quantities of hematopoietic factors that are known to be important are present in the recommended daily dose.

Vitamin B_{12} with Intrinsic Factor—When secretion of intrinsic factor in gastric juice is inadequate or absent (e.g., in Addisonian pernicious anemia or after gastrectomy), vitamin B_{12} in physiological doses is absorbed poorly, if at all. The resulting deficiency of vitamin B_{12} leads to the clinical manifestations of pernicious anemia. Similar megaloblastic anemias may develop in fish tapeworm (*Diphyllobothrium latum*) infection or after a surgically created small-bowel blind loop; in these situations, treatment requires freeing the host of the parasites or bacteria which appear to compete for the available vitamin B_{12}. Strict vegetarianism and malabsorption syndromes may also lead to vitamin B_{12} deficiency. In the latter case, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient.

Potency of intrinsic factor concentrates is determined physiologically, i.e., by their use in patients with pernicious anemia. The liver-stomach concentrate with intrinsic factor and the vitamin B_{12} contained in two Pulvules Trinsicon provide 1½ times the minimum amount of therapeutic agent which, when given daily in an uncomplicated case of pernicious anemia, will produce a satisfactory reticulocyte response and relief of anemia and symptoms.

Concentrates of intrinsic factor derived from hog gastric, pyloric, and duodenal mucosa have been used successfully in patients who lack intrinsic factor. For example, Fouts *et al.* maintained patients with pernicious anemia in clinical remission with oral therapy (liver extracts or intrinsic factor concentrate with vitamin B_{12}) for as long as twenty-nine years.

After total gastrectomy, Ficarra found multifactor preparations taken orally to be "just as effective in maintaining blood levels as any medication that has to be administered parenterally." His study was based on twenty-four patients who had survived for five years after total gastrectomy for cancer and who had been taking two Pulvules Trinsicon daily.

Folic Acid—Folic acid deficiency is the immediate cause of most, if not all, cases of nutritional megaloblastic anemia and of the megaloblastic anemias of pregnancy and infancy; usually, it is also at least partially responsible for the megaloblastic anemias of malabsorption syndromes, e.g., tropical and nontropical sprue.

It is apparent that in vitamin B_{12} deficiency (e.g., pernicious anemia), lack of this vitamin results in impaired utilization of folic acid. There are other evidences of the close folic acid-vitamin B_{12} interrelationship: (1) B_{12} influences the storage, absorption, and utilization of folic acid, and (2), as a deficiency of B_{12} progresses, the requirement for folic acid increases. However, folic acid does not change the requirement for vitamin B_{12}.

Iron—A very common anemia is that due to iron deficiency. In most cases, the response to iron salts is prompt, safe, and predictable. Within limits, the response is quicker and more certain to large doses of iron than to small doses.

Each Pulvule Trinsicon furnishes 110 mg. of elemental iron (as ferrous fumarate) to provide a maximum response.

Ascorbic Acid—Vitamin C plays a role in anemia therapy. It augments the conversion of folic acid to its active form, folinic acid. In addition, ascorbic acid promotes the reduction of ferric iron in food to the more readily absorbed ferrous form. Severe and prolonged vitamin C deficiency is associated with an anemia which is usually hypochromic but occasionally megaloblastic in type.

Contraindications and Precautions: Anemia is a manifestation that requires appropriate investigation to determine its cause or causes.

Folic acid *alone* is unwarranted in the treatment of pure vitamin B_{12}-deficiency states, such as pernicious anemia. Indeed, the use of folic acid in large doses in pernicious anemia without adequate vitamin B_{12} may result in hematologic remission but neurological progression.

As with all preparations containing intrinsic factor, resistance may develop in some cases of pernicious anemia to the potentiation of absorption of physiological doses of vitamin B_{12}. If resistance occurs, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential and are recommended.

In extremely rare instances, skin rash suggesting allergy has been noted following the oral administration of liver-stomach material. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Hemochromatosis and hemosiderosis are contraindications to iron therapy.

Adverse Reactions: In rare instances, iron in therapeutic doses produces gastrointestinal reactions, such as diarrhea or constipation. Reducing the dose and administering it with meals will minimize these effects in the iron-sensitive patient.

Dosage: One Pulvule twice a day. (Two Pulvules daily produce a standard response in the average uncomplicated case of pernicious anemia.)

How Supplied: Pulvules Trinsicon® (hematinic concentrate with intrinsic factor, Lilly), in bottles of 60 and 500 and in Identi-Dose® (unit dose medication, Lilly) in boxes of 100.

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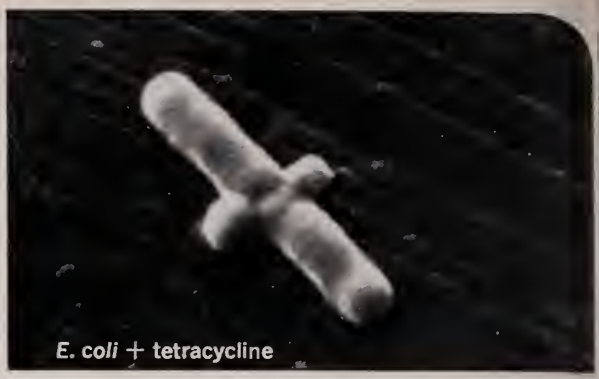
Encounter under the Scanning Electron Microscope



SEM reveals changes in *E. coli* exposed to antibacterial agents

The Scanning Electron Microscope (SEM) is the only instrument which gives 3-dimensional views on a microscopic level. This permits the surface morphology of microorganisms to be observed in detailed perspective. Changes in surface morphology of *E. coli* exposed to various antimicrobial agents are seen on the following page. An SEM photomicrograph of normal control *E. coli* appears above.









Different modes of antibacterial action — Similar changes in morphology

As part of a series of experiments,[1-3] strains of *E. coli* proven susceptible to each antibacterial agent were exposed to 1 MIC of the respective antibacterials for a three-hour period. Included were cell-wall-active drugs, ampicillin and cephalothin; a drug interfering with intracellular protein synthesis, tetracycline; and a chemical agent which acts by interference with para-aminobenzoic acid, sulfamethoxazole.

As seen above, elongation of the bacilli, mid-cell defects and spheroplast-like forms may be appreciated with the SEM technique. These changes in bacterial morphology were similar... regardless of the antibacterial agent used and irrespective of its mechanism of action.

"At present, the significance of these observations in clinical infection must be considered with caution, but it is hoped that these data will stimulate a reevaluation of present concepts of the nature and role of morphological variants of bacteria exposed to a variety of antibacterial factors."[2]

It should be noted that no clinical conclusions can be drawn from this study, as it is not always possible to extrapolate *in vitro* data to humans.

References: 1. Klainer, A. S.; Fass, R. J., and Perkins, R. L.: Scientific Exhibit presented at the 25th American Medical Association Clinical Convention, New Orleans, La., Nov. 28-Dec. 1, 1971. **2.** Klainer, A. S., and Perkins, R. L.: *Antimicrob. Agents Chemother.*, *1*:164, 1972. **3.** Klainer, A. S.: Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A t hemolytic streptococcal infections and will not eradicat o prevent sequelae (rheumatic fever, glomerulonephritis) of c infections. Deaths from hypersensitivity reactions, agranulo t sis, aplastic anemia and other blood dyscrasias have bee r ported and early clinical signs (sore throat, fever, pallor, pu or jaundice) may indicate serious blood disorders. Frequent B and urinalysis with microscopic examination are recomme e during sulfonamide therapy. Insufficient data on children u e six with chronic renal disease.

Precautions: Use cautiously in patients with impaired or hepatic function, severe allergy, bronchial asthma; in glu 6-phosphate dehydrogenase-deficient individuals in whom related hemolysis may occur. Maintain adequate fluid inta prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocyt

Encounter in Clinical Practice

Control of primary bacterial offenders

Antibacterial Gantanol® (sulfamethoxazole) controls susceptible strains of *E. coli* and other gram-negative and gram-positive organisms often implicated in acute nonobstructed pyelonephritis and cystitis.

Prompt antibacterial blood and urine levels

In from 2 to 3 hours after the initial 2-Gm adult dose, antibacterial levels are present in both the blood and urine.

B.I.D./T.I.D. dosage for around-the-clock coverage

Subsequent 1-Gm doses provide up to 12 hours of antibacterial coverage. More severe u.t.i. may require a q. 8 h. dosage regimen. Either schedule provides coverage during the waking and sleeping hours—especially important during hours of sleep when normal urinary retention tends to favor bacterial proliferation.

Also effective in nonobstructed chronic and recurrent u.t.i.

It is not uncommon for the elderly and the debilitated to develop chronic and/or recurrent nonobstructed urinary tract infections such as pyelonephritis and cystitis. Such cases often respond satisfactorily to Gantanol. The increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents including sulfonamides, especially in chronic or recurrent u.t.i.

Your Option: Tablets or Suspension

Either dosage form—the Tablets or the pleasant-tasting, cherry-flavored Suspension—can provide the dependable antibacterial activity necessary to control susceptible nonobstructed cystitis and pyelonephritis. Symptomatic improvement may usually be expected in 24 to 48 hours. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake. Gantanol (sulfamethoxazole) is generally well tolerated with relative freedom from complications; the most common side effects are nausea, vomiting and diarrhea. Frequent c.b.c.'s and urinalyses with microscopic examination are recommended.

In nonobstructed cystitis and pyelonephritis due to susceptible organisms

Gantanol®
(sulfamethoxazole)
Basic Therapy

---

stic anemia, thrombocytopenia, leukopenia, hemolytic ane-
purpura, hypoprothrombinemia and methemoglobinemia);
gic reactions (erythema multiforme, skin eruptions, epider-
necrolysis, urticaria, serum sickness, pruritus, exfoliative
natitis, anaphylactoid reactions, periorbital edema, conjunc-
and scleral injection, photosensitization, arthralgia and
gic myocarditis); *gastrointestinal reactions* (nausea, emesis,
minal pains, hepatitis, diarrhea, anorexia, pancreatitis and
natitis); *CNS reactions* (headache, peripheral neuritis, men-
lepression, convulsions, ataxia, hallucinations, tinnitus, ver-
and insomnia); *miscellaneous reactions* (drug fever, chills,
nephrosis with oliguria and anuria, periarteritis nodosa and
phenomenon). Due to certain chemical similarities with
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(Continued to page 1076)

Special Article

Acute Myocardial Infarction, 1970

Evaluation by Medical Audit in Five Minnesota Hospitals

WILLIAM R. FIFER, M.D.

INTERNAL MEDICAL AUDIT is being used by five Minnesota community hospitals to determine the continuing education needs of their medical staffs in a program sponsored by the University of Minnesota Division of the Northlands Regional Medical Program. The process involves six steps:

1. Setting standards of optimal achievable care for a given illness, operation, or condition. This function is performed by the medical staff audit (professional activities) committee.
2. Reviewing by the consecutive case method the actual care of that illness. This function is performed by review of displays of patterns of care prepared by the Medical Records Department.
3. Comparing optimal care with actual care to look for gaps, a function of the medical staff audit committee.
4. Translating these gaps into educational objectives which become the basis for the hospital's continuing medical education program. This is done by the medical staff education committee under the leadership of the Director of Continuing Medical Education.
5. Establishing "monitor parameters" for the illness studied to permit rapid evaluation of compliance with standards on a periodic basis. This procedure is set up by the audit committee.
6. Scheduling re-audit of the illness studied at an appropriate interval after the educational program, to see if learning (behavioral change) occurred. This step closes the loop to the beginning of the audit cycle.

Each of the five participating hospitals is encouraged to internalize the audit procedure so that they are working with their own standards, their own cases and their own education. The medical staffs are organized differently and have proceeded independently to select their choice of diseases to study. We have intentionally avoided suggesting external standards or some universal "gold standard" for each disease, because the process of standard setting is educational in itself.

As coordinator of their efforts, however, we could not resist the temptation to pool data for certain common diseases, hoping we would all learn more in the process than if each hospital made its own studies. Therefore, we decided to have each of the five medical staff audit committees respond to a list of 23 questions* about myocardial infarction to derive comparative and group standards, or "pattern criteria." We then reviewed all the cases of acute myocardial infarction in 1970 in the five participating hospitals to formulate comparative and group care patterns. Results of these comparisons are being reported here.

The important achievement is the *process* by which medical care is appraised—the *content* is incidental. We selected myocardial infarction because it is a common and serious disease in our society, and serves to display the practice patterns of Minnesota doctors in community hospitals. The data are crude, but as true as can be obtained by mass analysis techniques without reviewing every chart in detail. These crude data were fed back to each cooperating hospital to help them identify their own continuing education needs.

The Study Context

The five Minnesota Audit Hospitals in this year's program are scattered about the state in small (circa 10,000 population) cities. The smallest hospital has 17 medical staff members and 64 acute beds; the largest has 31 doctors and 185 acute beds. We have a total of 142 physicians and 663 acute beds to share data; a sizable community "teaching hospital" in a functional sense. Each hospital has a Director of Continuing Medical Education (DCME) one day a week. Three of the five hospitals are long-time subscribers to the PAS/MAP computer-assisted data storage and retrieval system sponsored by the Commission on Professional and Hospital Activi-

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*See Appendix, page 1075.

ties in Ann Arbor, Michigan. In those hospitals, we used only the computer-generated forms in reviewing care in this study. These forms greatly simplify record review, but allow a little "dirtier" data than when each medical record is reviewed completely. This is because PAS/MAP review assumes that each case listed as an acute myocardial infarction has satisfied enough diagnostic criteria to be so coded by the attending physician at the time of discharge. Such a review accepts the diagnosis as given, rather than examining the diagnostic process. When one reviews actual medical records, however, he begins to "toss out" cases included in that diagnostic code because, for example, the electrocardiographic charges are non-specific, and the rise in serum enzymes is equivocal. Any review of patient care is only as good as the medical record, and when such a review is based on PAS/MAP printouts, it also depends heavily on the accuracy of preparation of the case abstract by medical records personnel. One must carefully define the diagnosis of even such an apparently noncontroversial disease as myocardial infarction in order to assure uniformity of the data.

Presented, then, is a data display gleaned from PAS/MAP printouts alone, and the questions asked are limited to those which the PAS/MAP forms can answer. In so doing, we are only presenting one-third of the total information needed to appraise medical care, as we divided information needs into three parts: (1) that information which can be retrieved by medical records personnel (given the right questions by the medical staff) from PAS/MAP printouts; (2) that information which is retrievable by medical records personnel from the medical record itself (this includes many items in the history and physical examination); and (3) that information which only the medical staff can appraise, such as appropriateness of antibiotic therapy.

Our study included 424 cases, and represents all patients discharged from our five audit hospitals in calendar year 1970, with the exception of our smallest hospital, where we studied all of 1970 with ten months of 1971 to get a reasonable number of consecutive cases (78). One hospital did not have an intensive coronary care unit (ICCU) during 1970, and another had such a unit in operation for only half of the year. The composition of the medical staffs varies greatly and this, along with rules about ICCU care, affects such things as the consultation rate. Thus some of our hospital staffs are predominantly general (family) practitioners, while others consist mostly of specialists, with the internist assuming the care of medical illnesses of adults. Sometimes one or two internists function primarily as cardiologists, and care for all the patients with acute myocardial infarction. At times, the ICCU rules decided by the medical staff provide for mandatory consultation by a cardiologist in certain situations. In one hospital, a full-time, hospital-based internist is director of the ICCU. All of these variations tend to affect the behavior of the medical staff and show up as differences in such items as consultation rate. These local practice patterns tend to make data such as the consultation rate incomparable, but reinforce the importance of having each staff set its own standards and perform its own internal medical audit.

Pattern Criteria

As mentioned, we asked the audit committee of each of the five medical staffs to answer 23 questions in order to derive group and comparative pattern criteria.

Some questions (5, 7, 12 and 17) were answered virtually identically by all five audit committees indicating complete agreement on a standard. They all felt that 100% of the patients should have an electrocardiogram and a repeat unless they died within hours, an event which precludes a repeat or comparison tracing. They all felt that 95% to 100% of all patients with acute myocardial infarction should be treated in an ICCU. They agreed it was important to diagnose the anatomic site of the infarction (though as we shall see, most of the time they did not actually specify the site in their discharge diagnosis). Finally, they felt that all of these patients should have a chest Xray during their hospitalization.

Eleven questions provoked answers in substantial agreement, though not complete (questions 1, 2, 3, 6, 11, 11a, 13, 14, 20, 22 and 23). For example, all five committees agreed closely on the median length of stay (LOS) (average 21.4 days —range 20 to 24 days). They felt the death rate should range from 15% to 20% (average 18.6%). They believed that 5% to 15% (average 9%) of patients should require pacemaker utilization for optimal care. They believed steroid therapy would be required seldom (3% to 10%)

and felt the same way about antibiotics (2% to 10%).

Nine questions, however, produced answers which were in substantial disagreement. Representative questions from this group were:

4. Consultation percentage (10% to 100%).
8. Percent of patients treated with oxygen (50% to 100%).
9. Percent of patients treated with anticoagulants (30% to 90%).
10. Percent of patients treated with cardiac regulatory drugs (50% to 80%).
15. Percent of patients having a rectal or pelvic examination at some time during admission (0% to 100%).
19. Percent of patients receiving coronary vasodilator drugs (0% to 50%).

To answer these questions, the medical staff committees drew upon their knowledge and opinions regarding these matters, and since there continues to be controversy in medicine regarding issues such as the use of anticoagulant therapy in acute myocardial infarction, we cannot expect uniform opinions (standards) to emerge. Likewise, there must be differences of opinion as to whether giving oxygen benefits these patients (and why) or whether coronary vasodilators (such as nitroglycerine and its analogs) are contraindicated. Most doctors agree that coronary vasodilators are useful for the patient with angina or coronary insufficiency, and may use them until they are convinced the patient has indeed suffered a myocardial infarction, and then discontinue them. These discussions (and many more) provoked by criteria setting, are inherently educational to the medical staff committees.

Profiles of Care

We studied both PAS/MAP printouts (mostly) and patient records (less) from many perspectives to describe the profiles of care in these 424 patients in five hospitals. Their median age was 66 years and 67% of them were men. The length of stay (median) was 20.4 days, with a range of 17 to 25 days. The death rate average 23.8%, but varied significantly from 12.5% to 40%. The hospital with the highest death rate did not have an ICCU in operation during 1970. There was no correlation between the consultation rate and the death rate; in fact the hospitals with the lowest death rate (12.5%) and the highest death rate (40%) had very similar consultation rates (34% and 30% respectively). Also Hospital "D" with a low consultation rate (7.2%) had the second lowest death rate (17.8%) (Table 1). These data illustrate that process cannot always be translated to outcome.

TABLE 1
Acute Myocardial Infarction, 1970
Patterns of Care

Item	Hospital A	B	C	D	E	Ave.
Median LOS (Days)	18	21	25	21	17	20.4 Days
Death Rate (%)	22	40	12.5	17.8	26	23.8%
Consultation Rate (%)	42	30	34	7.2	2.6	23%

The use of ICCU's in Minnesota hospitals is widespread, with 105 in operation out of 165 short-term general hospitals. The Minnesota Heart Association, in cooperation with the Northlands Regional Medical Program, has operated excellent training centers for ICCU nurses in multiple sites. A cooperative study by 64 participating ICCU's reported a hospital mortality rate of 18.3% for all acute myocardial infarction patients from July 1, 1970 to July 1, 1971. In the four audit hospitals with ICCU's 86% of the acute myocardial infarction patients were treated in these units, and all these were monitored. When we determined what percent of patients admitted to ICCU's turned out to have an acute myocardial infarction, we found a consistent figure of 44% (43, 45 and 45). This agrees well with the cooperative study of the Minnesota Heart Association which found 41% of 5,791 patients admitted to 64 participating ICCU's proved to have an acute myocardial infarction. Such consistency of data is most useful in planning such resources as ICCU beds and their staffing requirements. A total of 50 patients in this study (11.4%) were not treated in ICCU's (in the four hospitals that had ICCU's) and the same number did not receive the benefit of monitoring. Of these 50, 12 (24%) died, but there was great variation (from 14% to 45%), and our numbers are too small in this study to assess the increased risk of not being admitted to an ICCU.

When it came to "working up" the acute myocardial infarction patient, our doctors varied a lot. Although 79% of the patients had enzymes studied (SGOT, LDH, CPK) the range was from 57% to 92%. The blood sugar was determined in only 64% of the patients, again with a wide range of 49% to 90%. Cholesterol and/or lipid profiles were determined in only 49% of these patients. Physician behavior seems not to have been unduly influenced by automated "packages" of lab tests in these five hospitals. We found that Hospital "D," with the highest curiosity about the

patient's blood sugar (90%) and enzymes (92%), had the lowest curiosity about his cholesterol and/or lipids (36%) (Table 2).

TABLE 2
Acute Myocardial Infarction, 1970
Patterns of Care

Item	Hospital A	B	C	D	E	Ave.
Enzymes (%)	79	51	85	92	88	79%
FBS (%)	55	49	75	90	50	64%
BUN (%)	50	49	75	88	63	65%
Chol. Lipids (%)	49	48	55	36	57	49%
Oxygen Ther. (%)	84	0*	73	38.5	76	54%

*Recording Error?

There was a great difference in the use of oxygen. While overall 54% of the patients received oxygen, its use varied from 38% to 84%. We believe sharing these data with our hospital staffs will make them ask, "What is the right answer?" and set in motion education efforts to find out.

Location of Infarct

What is physician behavior in regard to stating the anatomic site of myocardial infarcts and does it make any difference? In answering this latter question to devise pattern criteria, most staffs said "yes," but they do not diagnose the site very consistently on the face sheet. Again, there was a great variation in behavior: Hospital "A" specified the site 86% of the time, whereas Hospital "B" *did not* specify the site 87% of the time. Altogether, anterior wall infarct was the most common site specified (24%) but "site not specified" was even more common (46%). When we look at these data we see that different physicians must be using different electrocardiographic criteria for identifying the site, and these variances are compounded by how many different physicians read the tracings. Note in Table 3 that 27% of the infarcts in Hospital "A" were classified as "inferior," while Hospital "C" classified none as "inferior." Hospital "C" said 22% were "lateral" while Hospital "E" said none were. Hospital "A" said no "posterior," while Hospital "E" said 21% were posterior, and both of these hospitals showed a great tendency to classify site. Data like this suggest that until we have uniform criteria for specifying the anatomic site of an infarct applied uniformly by all physicians who read EKG's, we will never be able to derive any meaningful correlation between site and prognosis (or complications). The Minnesota Heart Association Cooperative Study found that anterior wall infarction represented 48% of their 2,403 cases, while 30% had inferior wall infarction and 22% were subendocardial. Their hospital mortality rate was: anterior 23.5%, inferior 18%, and subendocardial 8%. This indicates an apparent prognostic difference determined by site. The Minnesota Heart Association Study also shows that anterior wall infarcts tend to die in the ICCU 78% of the time rather than after they are transferred out of the unit. Subendocardial infarcts, however, seem to be under greater increased risk, proportionately, after they leave the ICCU. But obviously the *extent* of the infarction is likewise important in determining survival, because most ICCU deaths are due to "pump failure" (72% in the Minnesota Heart Association Study). After leaving the ICCU, however, (a time during which a quarter of the deaths occur, according to the MHA Study) dysrhythmia deaths became almost as frequent (43%) as pump failure deaths. These data suggest we should know both the site and extent of infarction to predicate the likelihood of death both during and after the ICCU stay.

TABLE 3
Acute Myocardial Infarction, 1970
Patterns of Care
Location of Infarct (Expressed as Percent)

	Hospital A	B	C	D	E	Average (Range)
Anterior	23.5	10	41	22	25	24 (10-41)
Posterior	0	0	12.5	5.4	21	8 (0-21)
Inferior	27	3	0	3.6	6.5	8 (0-27)
Lateral	4.7	0	22	1.8	0	5.7 (0-22)
Subendocardial	3.5	0	1	0	4	1.7 (1-4)
Multiple Sites	29	0	0	0	5	7 (0-29)
Not Specified	14	87	24	67	37	46 (14-87)

When we look for other coded diagnoses on the face sheet such as shock, congestive heart failure and dysrhythmias, we find them infrequently; yet study of charts indicated they were present much more often. Depending on one's definition of how many runs of premature ventricular contractions make a dysrhythmia, this diagnosis appears almost universal from a study of the "rhythm strips" in the ICCU nurse's notes. Likewise, our doctors rarely diagnosed "defibrillation" such that the record librarian could spot it and enter it as a codeable operation.

How often should physicians manage infarct patients to remain competent? Medical staffs should address themselves to such questions. The range of cases per doctor in our study in 1970 was from one to 24, and each of the four hospitals for which we have information had at least one medical staff member who cared for only one

case in that year. It seems likely that if six liver biopsies were to be done annually in a hospital with six physicians on the staff, the staff would get together, choose the most able among them to perform the procedure, and have him do all six rather than each doing one per year. From such a division of labor we might expect less complications and more proficiency.

Utilization review (retrospective) is a by-product of such a review of cases as this. We found considerable difference in "long stay" (over 30 days) patients from 26% in Hospital "C" to 6.5% in Hospital "E." These patterns remained consistent when we selected long stay patients with no secondary diagnoses, ranging from 12.5% in Hospital "C" to 0% in Hospital "E." Before we get carried away by the siren song of reduced cost through reduced utilization, however, we note that Hospital "C," with its long stay, produced the lowest death rate (12.5%) of all (Table 4).

TABLE 4
Acute Myocardial Infarction, 1970
Patterns of Care

Item	Hospital A	B	C	D	E	Total or Ave.
Percent of Long Stay (LOS > 30 Days) Pts.	—	13	26	8	6.5	13 (8-26)
Percent of Long Stay (LOS > 30 Days) Pts. With no Secondary Diag.	—	5	12.5	1.8	0	4.8 (0-13)
Death Rate Percent	22	40	12.5	17.8	26	23.8

Performance of rectal and pelvic examinations showed behavioral differences among the medical staffs of the hospitals in the study. In Hospital "C" 7% of the patients got rectal and 1% got pelvics. In Hospital "E," however, 30% of the patients got rectals. There is no "right" answer, but if the infarct patient presented with metastatic rectal carcinoma six months after his hospitalization, we would all be chagrined.

Seventeen percent of all these patients had an elevated blood sugar, but in only 40% of this group was diabetes diagnosed. It is known that transient hyperglycemia occurs occasionally immediately after an infarct, presumably due to adrenal medullary hyperactivity. It is also known that most ICCU patients have a "keep open" I.V. of 5% glucose running (in our series 74%). But until we have a chance to follow these patients, we should list "elevated blood sugar" on the problem list in order to make sure we satisfy ourselves regarding its investigation in future encounters with the patient.

Identifying Gaps

By comparing pattern criteria with profiles of care, medical staffs can identify "gaps" between what they consider optimal care and the actual care delivered. As seen in Table 5, in certain areas no gap exists. For example, the standard set for median length of stay was 21.4 days, and the actual median stay was 20.4 days. In some very important areas, significant gaps exist. For example, Hospital "B" thought its myocardial infarction death rate should be 15% and it proved to be 40%. Learning of such *outcomes* as a 40% death rate motivates a medical staff to look at the *process of care* to see if they can improve their figure, in the same way that a golfer who shoots 90 on a par 72 course analyzes his game to seek improvement in his score.

TABLE 5
Acute Myocardial Infarction, 1970
Identifying Gaps

	Ideal Criteria	Actual Pattern
Length of Stay	21.4	20.4
Death Rate, Hospital B	15%	40%
Cholesterol/Lipid, Hospital D	100%	36%
Chest Xray	100%	83%

Review of blood chemistries done in "working up" infarct patients also discloses major discrepancies between standards set and actual behavior. For example, Hospital "D" set as a pattern criterion the performance of cholesterol/lipid patterns in 100% of its myocardial infarction patients, but did so in only 36%. Gaps may exist for all hospitals within the study which "cancel out" when looked at as a group. This is seen in the use of anticoagulant therapy: The "group standard" was to administer anticoagulants to 68%, yet among the individual hospitals both positive and negative discrepancies exist between the standard set and the care delivered.

All five hospitals agreed that 100% of all myocardial infarction patients should have a chest Xray, based upon sound medical reasoning which seems universally shared, yet about 17% of those patients failed to get a chest Xray for one reason or another.

Educational Objectives

The audit committee, having identified gaps between optimal and actual performance, asks the education committee to translate these gaps into educational objectives to guide a program of hospital-based continuing medical staff education

based on demonstrated knowledge needs. The Director of Continuing Medical Education functions as staff to the education committee in implementing this continuing education program.

A sample educational objective might be: "Following a medical staff meeting devoted to learning the importance of lipid phenotypes and their treatment and the association of abnormal lipid metabolism to the risk of coronary atherosclerosis, the medical staff will determine cholesterol/lipids in 95% of all patients with acute myocardial infarction, and diagnose hyperlipidemia on the face sheet in 75% of the patients in whom it has been demonstrated."

One can easily formulate similar educational objectives related to these gaps: (Table 6)

(1) Fourteen percent of the patients in these five hospitals never get into the ICCU.
(2) Fifty percent of these patients in Hospital "E" did not have blood glucose determined.
(3) Forty-nine percent of these patients in Hospital "B" did not have enzymes determined.
(4) Sixty-two percent of these patients in Hospital "D" did not receive oxygen therapy.
(5) Eighty-seven percent of the infarcts at Hospital "B" were diagnosed as "site not specified."
(6) Twenty-three percent of the myocardial infarction patients in Hospital "D" did not have a chest Xray during their admission.

TABLE 6
Acute Myocardial Infarction, 1970
Educational Objectives

1. **Get all patients into the ICCU (14% did not).**
2. **Get blood sugar in all MI patients (50% did not).**
3. **Get enzymes on 100% (49% in Hospital B did not).**
4. **Give oxygen therapy to all patients (62% in Hospital D did not get oxygen therapy).**
5. **Specify the site 100% of the time (87% in Hospital B were diagnosed as "site not specified.")**
6. **Get chest Xrays in all (23% in Hospital D did not get chest Xrays).**

Some gaps (knowledge needs) are common to all five hospitals, while others are limited to one or two. Each educational program must be individually tailored to meet the knowledge needs of the hospital.

The medical audit system used in this study provides a means of objectively evaluating the education program in terms of behavioral change by simply re-auditing myocardial infarction care (or any specific element of it) at a suitable interval after the education effort. We know from our 1970 study that only 36% of the acute myocardial infarction patients in Hospital "D" had cholesterol and/or lipids determined. After Hospital "D" conducts an education program whose objective is to increase this level of determinations, the level will either go down, stay the same, or go up. Only with the latter result can one claim that the education program modified physician behavior favorably.

Summary

We have presented a look at the use of internal medical audit to determine continuing medical educational needs in five community hospitals in Minnesota—using a study of all myocardial infarction patients in these hospitals in 1970 as an example. There are limitations to using PAS/MAP printouts alone to garner such statistics: These limitations are related to: (1) the accuracy of input (the case summary prepared by the medical records personnel) and (2) the acceptance of the diagnosis as given without critically examining the evidence upon which it is based.

Such a study, however, displays gaps which the individual hospital medical staffs may wish to pursue by appraisal of all or any part of such a subject as myocardial infarction. We believe these displays of patterns of care prepared by medical records personnel permit the medical staff audit committee to "zero in" on problem areas. Busy doctors cannot take the time away from patient care to review all 424 cases of myocardial infarction by reviewing every single chart. They can, by learning to review patterns of care, select those cases, those areas, which require further analysis to improve care of this disease in their institution by applying *directed* continuing education.

We have little ability to study *diagnostic outcomes* or *process* by this method, but we feel satisfied that such an audit as the one presented does identify some *therapeutic outcomes* and scrutinizes the *therapeutic process* in considerable detail. It permits the medical staff to "take inventory" of specific areas of care, and allows them to select "critical incidents" of care for study by review of the entire medical record.

This study illustrates how the medical staff of the community hospital can determine its knowledge needs to construct a relevant, on-site pro-

gram of continuing education whose effectiveness can be evaluated by re-audit after the educational effort has occurred. We hope studies like this also provide feedback to medical educators who have often constructed curricula with little information about the actual behavior of physicians in community hospitals.

APPENDIX

Pattern Criteria for Acute Myocardial Infarction

1. What percent of the patients we admit to the ICCU should turn out to have an acute myocardial infarction?
2. What should be the median (50th percentile) stay for acute myocardial infarction patients?
3. What should the death rate be?
4. What percent of acute myocardial infarction patients should have consultation?
5. What percent should have an electrocardiogram? A repeat electrocardiogram?
6. What percent should have:
   - A. Fasting blood sugar
   - B. BUN
   - C. Enzymes
   - D. Cholesterol/lipids
7. What percent of patients should be in the ICCU?
8. What percent should receive oxygen therapy?
9. What percent should receive anticoagulant therapy?
10. How often should cardiac regulator drugs be used?
11. How often should defibrillation be needed?

11a. How often should closed-chest cardiac massage be needed?

12. Is it important in the clinical management of the infarct patient or in his prognosis that we identify the anatomic site of the infarct?
13. How often should pacemakers be needed?
14. How often should patients stay beyond 30 days with no other coded diagnoses?
15. What is the significance of hypertension on admission? How common is it?
16. How often should we do rectal/pelvic examinations on a patient with acute myocardial infarction at any time during their admission?
17. How often should we do chest Xrays on acute myocardial infarction patients?
18. Are there times you would not like to put a patient in the ICCU? If so, would you monitor such a case on the open wards?
19. What are the indications or contraindications for the use of coronary vasodilator drugs in the patient with acute myocardial infarction? How often should they be used?
20. What are the indications for steroid therapy in acute myocardial infarction patients? How often would we expect them to be used in our hospital?
21. What are the indications for diuretic therapy in acute myocardial infarction patients? How often would we expect them to be used in our hospital?
22. What are the indications for antihypertensive therapy in acute myocardial infarction patients? How often would we expect them to be used in our hospital?
23. What are the indications for antibiotic therapy in acute myocardial infarction patients? How often would we expect them to be used in our hospital?

We never cast our eyes towards "Harrow on the Hill" (let us keep these picturesque denominations of place as long as we can) without thinking of an amiable man and most pleasant wit and physician of Queen Anne's time, who lies buried there—Garth, the author of the *Dispensary*. He was the Whig physician of the men of letters of that day, as Arbuthnot was the Tory: and never were two better men sent to console the ailments of two witty parties, or show them what a nothing party is, compared with the humanity remaining under the quarrels of both.*

*Leigh Hunt, "Garth, Physicians, and Love-Letters," in Men Women and Books, 1847.

Meeting

MEDICAL AUDIT & PROBLEM-ORIENTED RECORD, Office of Postgraduate Medical Education, U of M & Northlands Reg. Medical Program, Nolte Center for Continuing Education, Minneapolis. November 10 and 11. Accreditation: 8½ hours of elective credit. Fee: $65 (physician *or* Medical record administrator); $95 (physician *and* Medical record administrator). Contact: Mr. Stephen Rogness, Minesota Hospital Association, 2333 University Ave. S.E., Minneapolis 55414.

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minnesota medicine



al Wonderland"

Vernon L. Lindberg, M.D.

DECEMBER, 1972

Section 1 of Two Sections



Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

Before deciding to make Valium (diazepam) part of your treatment plan, check on whether or not the patient is presently taking drugs and, if so, what his response has been. Along with the medical and social history, this information can help you determine initial dosage, the possibility of side effects and the ultimate prospects of success or failure.

While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

Complete literature available on request from Professional Services Dept. PML.

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The Advertising Pays for Your Journal

hould old depressives be forgot?

giatric depressive.
Uable to concentrate he tends
lk ittle interest in the affairs
in him. His reactions are slow
layed. He speaks very little.
n e does, it's mostly to com-
his insomnia, fatigue, or
t ation.

One way of relieving depression in the geriatric patient is with Tofranil.

Please read the prescribing information for details of usage (lower dosages are recommended for elderly patients and adolescents), precautions, warnings, contraindications, adverse experiences, and dosage recommendations. It is summarized below.

Tofranil® Geigy
imipramine hydrochloride USP



mipramine hydrochloride USP

ications: The concomitant use of this agent amine oxidase inhibiting (M.A.O.I.) com- contraindicated. Hyperpyretic crises or ivulsive seizures may occur. Potentiation of fects can be serious or even fatal. An interval 14 days after M.A.O.I. therapy has been ed should be allowed before this drug may uted. Initial dosage should be low, increases gradual, and the patient's progress should ly observed. The drug is also contraindicated the acute recovery period after myocardial . (b) in patients with known hypersen- the drug. Cross-sensitivity to other dibenz- mpounds should be kept in mind.

nings: *Usage in Pregnancy:* Safe use of ne during pregnancy and lactation has not blished; therefore, in administering the drug nt patients, nursing mothers, or women of ing potential, the potential benefits must be against the possible hazards. Animal repro- tudies have yielded inconclusive results. ve been clinical reports of congenital mal- n associated with the use of this drug, but a lationship has not been confirmed. eme caution should be used when this drug o:

s with cardiovascular disease because of the ility of conduction defects, arrhythmias, rdial infarction, strokes and tachycardia; ts with increased intraocular pressure, history ary retention, or history of narrow-angle ma because of the drug's anticholinergic ties;

hyroid patients or those on thyroid medica- cause of the possibility of cardiovascular y;

ts with a history of seizure disorder because ug has been shown to lower the seizure old;

ts receiving guanethidine or similar agents mipramine may block the pharmacologic of these drugs.

ge in Children: Pending evaluation of results ical trials in children, the drug is not recom- for use in patients under twelve years of age. e the drug may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as operating an automobile or machinery, the patient should be cautioned accordingly.

Precautions: Because of the possibility of suicide in seriously depressed patients, careful supervision during the early phase of treatment is necessary and hospitalization may be required. Prescriptions should be written for the smallest amount feasible.

Hypomanic or manic episodes may occur, particularly in patients with cyclic disorders. Such reactions may necessitate discontinuation of the drug. If needed, imipramine may be resumed in lower dosage when these episodes are relieved. Administration of a tranquilizer may be useful in controlling such episodes.

Prior to elective surgery, imipramine should be discontinued for as long as the clinical situation will allow.

An activation of the psychosis may occasionally be observed in schizophrenic patients and may require reduction of dosage and the addition of a phenothiazine.

In occasional susceptible patients or in those receiving anticholinergic drugs (including antiparkinsonism agents) in addition, the atropine-like effects may become more pronounced (e.g. paralytic ileus). Close supervision and careful adjustment of dosage is required when this drug is administered concomitantly with anticholinergic or sympathomimetic drugs.

Patients should be warned that the concomitant use of alcoholic beverages may be associated with exaggerated effects.

Both elevation and lowering of blood sugar levels have been reported.

Concurrent administration of imipramine with electroshock therapy may increase the hazards; such treatment should be limited to those patients for whom it is essential.

Adverse Reactions: *Cardiovascular:* Hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block, stroke, falls.

Psychiatric: Confusional states (especially in the elderly) with hallucinations, disorientation, delusions; anxiety, restlessness, agitation; insomnia and nightmares; hypomania; exacerbation of psychosis.

Neurological: Numbness, tingling, paresthesias of extremities; incoordination, ataxia, tremors; peripheral neuropathy; extrapyramidal symptoms; seizures, alterations in EEG patterns; tinnitus.

Anticholinergic: Dry mouth, and, rarely, associated sublingual adenitis; blurred vision, disturbances of accommodation, mydriasis; constipation, paralytic ileus; urinary retention, delayed micturition, dilation of the urinary tract.

Allergic: Skin rash, petechiae, urticaria, itching, photosensitization (avoid excessive exposure to sunlight); edema (general or of face and tongue), drug fever, cross-sensitivity with desipramine.

Hematologic: Bone marrow depression including agranulocytosis; eosinophilia; purpura; thrombocytopenia. Leukocyte and differential counts should be performed in any patient who develops fever and sore throat during therapy; the drug should be discontinued if there is evidence of pathological neutrophil depression.

Gastrointestinal: Nausea and vomiting, anorexia, epigastric distress, diarrhea; peculiar taste, stomatitis, abdominal cramps, black tongue.

Endocrine: Gynecomastia in the male; breast enlargement and galactorrhea in the female; increased or decreased libido, impotence; testicular swelling; elevation or depression of blood sugar levels.

Other: Jaundice (simulating obstructive); altered liver function; weight gain or loss; perspiration; flushing; urinary frequency; drowsiness, dizziness, weakness and fatigue; headache; parotid swelling; alopecia.

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How Supplied: Round tablets of 25 and 50 mg.; **triangular** tablets of 10 mg. for geriatric and adolescent use; and ampuls, each containing 25 mg. in 2 cc. for I.M. administration. (B)98-146-850-H (7/71)

For complete details, including dosage, please refer to the full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

TO 8575



When you select this familiar antibiotic for IV infusion you have available a broad dosage rang that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administere intravenously to adults.

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Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

ifections caused by susceptible strains
pneumococci, streptococci, and
aphylococci, including penicillin-
sistant strains. Staphylococcal strains
sistant to Lincocin (lincomycin
ydrochloride, Upjohn) have been
covered. Before initiating therapy,
alture and susceptibility studies should
performed. Lincocin has proved
luable in treating patients hyper-
nsitive to penicillin or cephalosporins,
nce Lincocin does not share
tigenicity with these compounds.
owever, hypersensitivity reactions
ve been reported, some of these in
tients known to be sensitive to
nicillin.

ell tolerated at infusion site: Lincocin
travenous infusions have not
oduced local irritation or phlebitis,
hen given as recommended. Lincocin
usually well tolerated in patients who
e hypersensitive to other drugs.
evertheless, Lincocin should be used
utiously in patients with asthma or
gnificant allergies.

patients with impaired renal function,
e recommended dose of Lincocin
ould be reduced to 25—30% of
e dose for patients with normal
dney function. Its safety in
egnant patients and in infants
ss than one month of age has
t been established.

incocin may be used with other
timicrobial agents: Since Lincocin
stable over a wide pH range, it is
itable for incorporation in
travenous infusions; it also may be
administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatme
Skin and mucous membranes—Skin rash urticaria, vaginitis, and rare instances of foliative and vesiculobullous dermatitis h been reported. *Liver*—Although no direct lationship to liver dysfunction is establish jaundice and abnormal liver function te (particularly serum transaminase) have b observed in a few instances. *Cardiovascu*—Instances of hypotension following par teral administration have been report particularly after too rapid IV administ tion. Rare instances of cardiopulmonary rest have been reported after too rapid administration. If 4.0 grams or more adm istered IV, dilute in 500 ml of fluid a administer no faster than 100 ml per ho *Special senses*—Tinnitus and vertigo h been reported occasionally. *Local reacti*—Excellent local tolerance demonstrated intramuscularly administered Lincoc (lincomycin hydrochloride). Reports of p following injection have been infreque Intravenous administration of Lincocin 250 to 500 ml of 5% glucose in distill water or normal saline has produced local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 m* Capsules—bottles of 24 and 100. *Ster Solution, 300 mg per ml*—2 and 10 ml vi and 2 ml syringe. *Syrup, 250 mg per 5* —60 ml and pint bottles.

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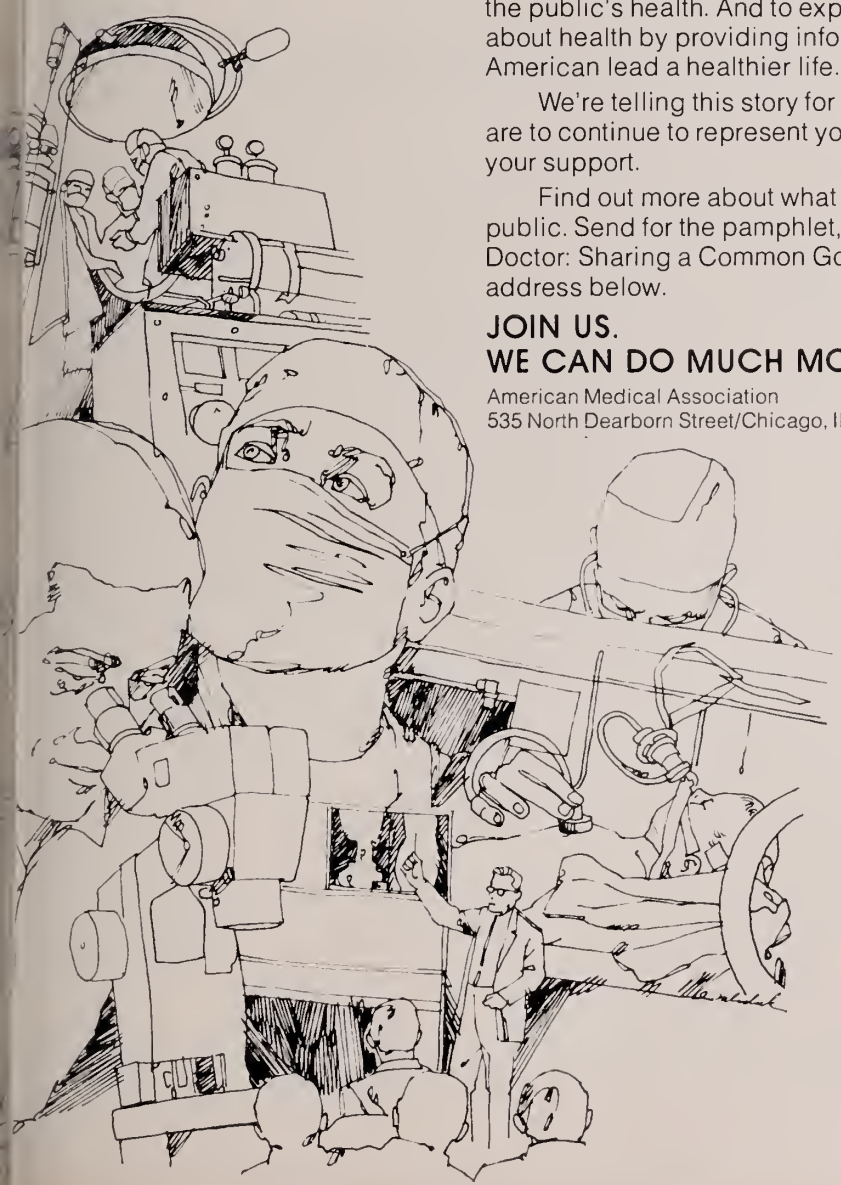
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President's Letter



Christmas Gift

THE FIRST GREETING on Christmas Day in our family is "Christmas Gift," a tradition originating from the Kentucky background of my father. It has come to be a greeting and expression of good will rather than its prosaic meaning, almost as if to say "The Gift of Christmas to you."

During the Advent Season, our schedules are full and often the Gift of Christmas, which in essence can be theistic as well as atheistic, is lost. "Peace on Earth, goodwill towards men" is a goal we should not shun.

It is my hope that our Association can be the originator of many Gifts of Christmas during the coming months through our activities. One way to support this effort would be for dedicated humanitarian physicians to serve on our Association's committees, which are the grass root origins of our policies, dedicated to promoting better medical care for Minnesotans.

Will you join with me in spreading the essence of Christmas? It could help everyone's New Year to be richer.

"Christmas Gift"

George B. Fratten

President
Minnesota State Medical Association

With the means at hand to drastically reduce the number of deaths each year from uterine cancer, we have embarked on a nationwide, life-saving program. Its goal is a Pap test by 1976 for every woman 20 years or older to whom the test is applicable, and for younger women at risk. An ambitious program, doctor, and one which can only be realized with your help.

We are faced with these facts: only 53% of women over 20 have ever had a Pap test; only 20% get a Pap test periodically; each year about 43,000 new cases are diagnosed; this year 12,000 women in this country will die of uterine cancer. And about 75% of these deaths will result from cervical cancer—as you know, almost 100% curable when diagnosed early and treated promptly.

We hope to reach women in the target group not only with the message about the *vital* Pap test, but also with the urgency of including it in the *regular* health checkup. The mortality rate from uterine cancer could thus be dramatically curtailed.

Clearly action is called for. Coordinated action—involving the doctor, the patient, the American Cancer Society—a partnership for life.

a partnership for life



THIS SPACE CONTRIBUTED BY THE PUBLISHER AS A PUBLIC SERVICE

"The history of science, and in particular the history of medicine . . . is . . . the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

– George Sarton, from "The History of Medicine Versus the History of Art"

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion

Results of a questionnaire to 7,000 physicians:

62.9%
Believe combination drug products are useful.

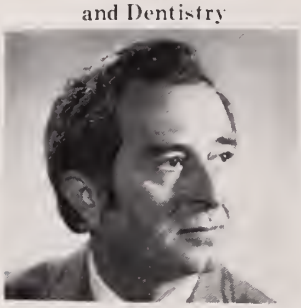
13.8%
Do not believe combination drug products are useful.

Are combination drug products useful in treatment involving concomitant use of two or more drugs?

Opinion & Dialogue

Doctor of Medicine

Louis Lasagna, M.D.
Professor and Chairman
Department of
Pharmacology & Toxicology
University of Rochester
School of Medicine
and Dentistry



Obviously, many drugs are given concomitantly. Whether it makes sense to combine medications in one preparation, be it capsule, tablet, or liquid, is a question that can be answered only by examining the advantages and disadvantages in the individual case.

Among the advantages is, first of all, convenience. The more medications that are taken concurrently and the more complicated the directions, the less likely the patient is to take medications accurately. From the standpoint of convenience and accuracy, and economy as well, you can make an important case for putting medications together in one preparation, as long as they are compatible.

By the same token, when you prescribe a properly tested and rational combination, you should have less worry about pharmaceutical or pharmacological compatibility — and about reasonable dosage ratios as well. Compatibility of the formulation should be demonstrated in the laboratory and clinic before the product is available for prescription—which is more than can usually be said for the physician's own spontaneous creations. And, the dosage ratios employed in rational precompounded combinations are designed to meet the needs of substantial numbers of "typical" patients.

There is no doubt that many "atypical" patients are to be found, and for them the prefabricated combination must be rejected. But that hardly argues for eliminating rational combinations from the market. Think, for example, of the problems that would arise if the components of widely accepted combinations, like the oral contraceptives and the diuretic-antihypertensives, always had to be prescribed, purchased and ingested separately.

One disadvantage that comes to mind is some doctors' unawareness of the ingredients a given combination contains. For example, a doctor might know that a patient is allergic to aspirin but forget that a certain analgesic mixture, which he knows only by its trade name, contains aspirin. His prescription, then, causes considerable discomfort, to say the least. This problem is a function of physician education, rather than of combination therapy as such. Improving doctors' knowledge about all medicaments they prescribe is a problem that deserves tackling on its own.

Another accusation leveled at combination drugs is that they encourage sloppiness of diagnosis and treatment. In many cases, however, a combination may prove to be the most effective choice. A good example of the usefulness of combinations appears in a recent article in the *Journal of Chronic Diseases* on the efficacy and side effects of an antihypertensive containing three ingredients, in which the track records of the combination drug and the individual ingredients were compared. Interestingly enough, whether the drugs were given individually or together, incidence and severity of side effects were the same. But blood pressure control was invariably better when the drugs were taken in one combination tablet than when they were taken separately (in "titratable" dosage) or in two or three different tablets.

Deciding which combinations constitute rational therapy obviously leads to a discussion of who is to determine which should be used and which should not. Realistically, I think combinations should be evaluated somewhat differently if they are old and established or new and untried.

In today's regulatory atmosphere, there is no possibility of a new combination being put on the market without a substantial amount of acceptable evidence in the form of controlled trials that show it to be safe and efficacious. On the other hand, I believe a different set of standards should apply to combination preparations that have been around for a long time. In other words, physician acceptance over a long period should be given some weight as evidence of the efficacy and safety of these drugs.

The FDA, however, does not seem to share this attitude. It often requires, for these older products, controlled trials that will monopolize the time of already overtired investigators and cost a great deal of money. I wish we could agree on a "grandfather clause" approach to many combinations that have been around for a number of years and that have an apparently satisfactory track record.

For example, I think some of the antibiotic combinations that were withdrawn off the market by the FDA performed quite well. I am thinking particularly of the penicillin - streptomycin combinations that physicians—especially surgical patients—were given by injection. This made for less discomfort for the patient, less demand on nurses' time, and fewer opportunities for dosage errors. To take such a preparation off the market doesn't seem to be good medicine, unless actual overdosage showed a great deal more harm from the injection (rather than the proper use) of the combination.

The point that should be emphasized is that there are both rational and irrational combinations. The real question is, who should determine which is which? Obviously, the FDA must play a major role in assessing this determination. In fact, I don't think it can avoid taking the ultimate responsibility, but it should enlist the help of outside physicians and experts in assessing the evidence and in making the ultimate decision.

Maker of Medicine

. Clarke Wescoe, M.D.
President
inthrop Laboratories



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combinations generally. Obviously, no one should be exposed willy-nilly to the potential side effects of two or three antihiotics when only one is needed. At the same time there are cases where it is prudent to prescribe more than one. The clinician is the judge in these circumstances, as he should be.

There is no clear definition of the word rational. Most persons, I suppose, would find it synonymous with reasonahle, hut in many circumstances it may best be defined as the opinion of those in power at the moment.

Other factors govern combination therapy, not the least of which has heen its broad use by practicing physicians anxious to achieve convenience in prescribing, to reduce medication error, and to save money for their patients. Combinations clearly have met the test on all three counts.

I have been impressed hy studies showing that the rate of error climhs markedly with the numher of medications to be taken, even with sophisticated patients. When medically justified, therefore, this factor alone supports the logic of comhination therapy.

The cost argument for combinations appears to be irrefutahle. In 1971, R. A. Gosselin studied the 71 combination products (excluding oral contraceptives) among the 200 most prescribed drugs. The study found that if all 71 products were discontinued, and if each ingredient in these combinations were prescribed separately, the price of medicines to patients would jump by $443.2 million on a national basis! At a time when the cost of medical care is under so much fire, it would be nonsensical to boost costs without clearly irrefutable medical reasons.

The part played by government on this question, of course, is fundamental. The FDA should play a role in determining which comhinations are reasonable. That role, as defined by law and regulation, is to ensure that any medication on the market is safe and effective in line with its label claims. Certainly combinations are entitled to as much consideration as single entities—neither more nor less. So long as the addition of one drug to another does not make either less safe, or less effective, so long as they are compatihle in a formulation, we have a reasonable product. It makes no sense to recommend the use of two products for certain conditions and to deny their being combined in a single form. An unhappy side effect of the prohlem concerns the efficacy panel discussions of many products submitted for review. The term "effective, but" has been freely interpreted to mean "ineffective" in toto, regardless of the merit of the individual drugs. This interpretation has placed numerous useful comhination products in needless jeopardy.

In reading the actual reports of the review panels, it seems clear that some of the ratings were based less on scientific research and clinical observation than on the "informed" opinions of the panelists. These "informed" opinions were accepted at face value, while the "informed" opinions of others who had used the products were rejected. All of this put combination products into a sort of scientific never-never land.

It should be kept in mind hy all, government as well as others involved in our health care system, that advances in therapy are seldom made in leaps and hounds hut rather by small painstaking steps—and that some of these steps have resulted from research in combination drugs as well as with single entities. Given the near-infinite biologic variation in patient response, this is hardly surprising to clinicians. It should not be to regulatory agencies either.

In the end, the practicing physician is in the best position to decide if a particular comhination makes sense. Such a decision should not he made exclusively by those whose responsihility for continuing clinical care is limited. Clinicians are the best judges of efficacy because the ultimate proof of any product's effectiveness is acceptance by phvsicians who have observed its actions in patients over time. The corollary statement may be made about over-the-counter medicines, which would not long survive if they failed to afford the relief the user anticipates. That the antihistamine in a "cold" remedy may not *always* be necessary is no reason to proscribe the combination generally.

Opinion & Dialogue

What is your opinion, doctor?
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Toxic Epidermal Necrolysis (Scalded Skin Syndrome)

Associated with Staphylococci

KRISHNA M. SAXENA, M.D. AND A.S. SETHI, M.D.

TOXIC EPIDERMAL necrolysis (scalded skin syndrome) as a separate entity was first described by Lang and Walker[1] and Lyell[2] in 1956. The association with staphylococcal infection has been well documented by the recent work of Melish and Glasgow.[3,4]

Our recent observation of six cases in two years suggests that the condition may be more common than the reports listed in the literature indicate. The disease usually starts as a tender skin lesion preceded or followed by marked erythema resembling scalded skin. Separation of the epidermis by slight pressure (Nikolsky sign) appears as a characteristic feature of the syndrome in the next 48 hours. Desquamation of the skin in large sheets follows, leaving wet raw areas which heal without scar formation. A purulent conjunctivitis is often present.

Thirteen cases of 'scalded skin syndrome' have been seen at the Children's Hospital during the last six years, six of them in the last two years. There were 10 females and three males between 14 days to three and a half years of age (Table 1). Seven children were younger than six months, four less than one month of age. All but three cases had some preceding infection, eight cutaneous, one otitis media and two upper respiratory. No patient had a history of drug ingestion prior to the illness.

The distribution of lesions is illustrated in Table 2. The face was the commonest site of involvement. Bullae were seen in six cases. Nikolsky's sign was positive in all cases. Fever was present in 11 patients, three of whom were also 'toxic.' Six children had purulent conjunctivitis. No other mucosal lesions were seen. Leucocytosis occurred in eight patients.

All were treated with antibiotics for staphylococcal infection. In one child, improvement was evident before the start of antibiotic therapy. Complete recovery occurred in all children. The illness lasted from five to 20 days. The mean duration was 10.5 days.

Coagulase positive staphylococci were cultured from the skin in 11 of the 13 cases. In nine of these patients the organism was also cultured from other sites usually the throat (Table 3). Coagu-

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Reprint requests to: Dr. K. M. Saxena, Children's Hospital, 311 Pleasant Avenue, St. Paul, Minnesota 55102.

TABLE 1
Clinical Features: Age, Sex & Preceding Lesions

Case No.	Age	Sex	Duration Of Illness	Preceding Lesions
1.	6 months	F	6 days	Pustular skin lesion
2.	14 days	F	10 days	Skin bullae
3.	14 days	F	20 days	Nil
4.	42 months	F	10 days	Fever + skin vesicles
5.	21 days	F	5 days	Pustular lesions
6.	18 months	M	10 days	U.R.I.
7.	36 months	F	8 days	Otitis Media
8.	6 months	M	12 days	Pustular lesion
9.	12 days	F	15 days	Pustular skin lesion, mastitis
10.	24 months	F	10 days	Impetigo
11.	6 months	F	10 days	Nil
12.	12 months	M	10 days	Nil
13.	20 months	F	8 days	Pustular skin lesion, rhinorrhea

lase positive staphylococci were cultured from the eyes in three cases, and stools in two. Phage-typing was possible in only four of the recent cases. All showed group II staphylococci of phage types 55/71/3C/3A/53.* The same phage types were seen in cultures obtained from different sites in Cases 10, 11, 12 and 13.

Summary of two representative cases is briefly presented.

Case Reports

Case 11

A six-month-old female was admitted on August, 1970. Her illness had started with redness around the eyes, proceeding to a conjunctivitis by the next morning. On the third day of the illness, erythema was also seen around the mouth, the nose and neck. On the fourth day, a markedly tender erythema was present all over the face, arms, trunk and legs up to the knees. On the same day, desquamation was seen on the forehead. By the nex day, desquamation was widespread and Nikolsky sig was positive. Peeling of the skin was more evident in th axillae, the neck and around the mouth. The skin aroun the mouth had the pursestring-like appearance char acteristic of this syndrome (Figures 1 and 2). Throughou this time, the child was febrile with a temperature o 37.8°C to 38.4°C. About the eighth day of illness heal ing was evident, the Nikolsky Sign became negative an the fever disappeared. No leucocytosis was seen durin the illness. Her IgG level was 120 mg% (normal for he is 200-660 mg%). Her IgM level was normal. Serun albumin and electrolytes were normal.

Coagulase positive staphylococci—group II—phag 79/3C/71/53 were cultured from her skin from thre different sites—ear, axillae and neck. Similar phage type were also cultured from the throat and stool, but blood culture was negative. One of her siblings who had scalp lesions also grew the same coagulase positive phag 79/3C/71/53 staphylococci.

Treatment was begun with saline soaks and I.V. Methicillin in a dose of 200 mg/kg/day. Later oral oxacillin was substituted for the antistaphylococcal antibiotic treatment which was continued for a total of nine days.

*Phage typing was kindly done by Dr. Adnan Dajani, University of Minnesota.

TABLE 2
Clinical Features: Distribution of Lesions

No.	Distribution	Bullae	Fever	Nikolsky	Leucocytosis
1.	Back, neck, face, groin, chest	Present	Present	Positive	Absent
2.	Face, abdomen, legs	Absent	Present	Positive	Present
3.	Face, neck, groins, limbs	Absent	+ Toxic	Positive	Present
4.	Antecubital fossa, abdomen groin, labia	Absent	+ Toxic	Positive	Absent
5.	Abdomen, thighs	Absent	Nil	Positive	Present
6.	Penis, face, all body	Occasional	Nil	Positive	Present
7.	Neck, chest, abdomen, face, eye	Occasional	Present	Positive	Present
8.	Face, arms, legs	Absent	Present	Positive	Present
9.	Abdomen, limbs, eyelids, chest	Absent	Present	Positive	Present
10.	Face, neck, groins, axillae, abdomen	Absent	+ Toxic	Positive	Absent
11.	Face, neck, extremities, groin axillae, abdomen, back	Occasional	Present	Positive	Absent
12.	Face, neck, axillae, trunk, groin, mid thighs, eye	Present (flaccid)	Present	Positive	Present
13.	Face, neck, axillae, trunk, groins, legs, arms	Present	Present	Positive	Absent

TABLE 3
Type of Staphylococci from Different Culture Sites

Case No.	Sites of Culture	Organism	Coagulase	Phage Type
1.	Skin	Staph.	Coag. Neg.	—
2.	Skin	Staph.	Coag. Pos.	—
3.	Skin, N.P.*, stool, cord	Staph.	Coag. Pos.	—
4.	Skin	Staph.	Coag. Pos.	—
5.	Skin, N.P.*, stool, cord	Staph.	Coag. Pos.	—
6.	Skin, N.P.*	Staph.	Coag. Pos.	—
7.	Skin, eye, throat	Staph.	Coag. Pos.	—
8.	Skin, N.P.*,	Staph.	Coag. Neg.	—
9.	Breast area, umbilicus, eye	Staph.	Coag. Pos.	—
10.	Skin	Staph.	Coag. Pos.	55
11.	Skin, scalp, stool, N.P.*	Staph.	Coag. Pos.	79/3C/71/53
12.	Skin, eye, ear, N.P.*	Staph.	Coag. Pos.	3A/3C/55/71
13.	Skin, lip, N.P.*	Staph.	Coag. Pos.	3C/55

*N.P.—nasopharynx

omplete healing of the conjunctivitis and skin lesions ccurred within 10 days.

ase 12

A one-year-old male child was admitted with a history f generalized erythema with desquamation, fever and ritability of two days duration. The illness started with eri-oral redness which soon progressed to tender ery- hema of the whole trunk, associated with fever of 39.6°C.

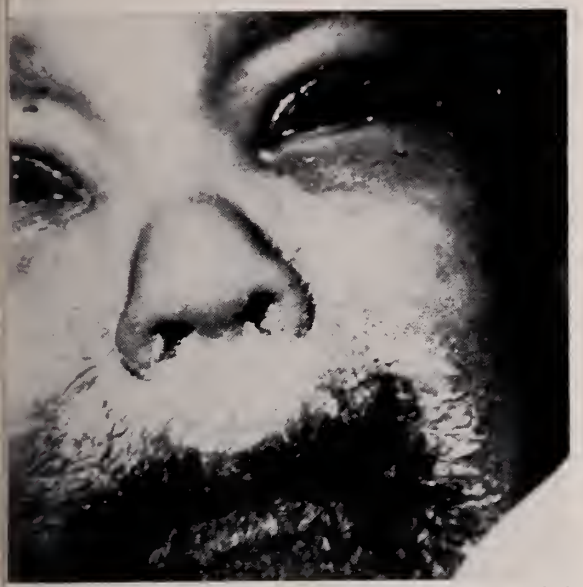


Fig. 1—Note the flaking, crusting lesions and denuded issures around the mouth. Purulent conjunctivitis was lso present in this child.



Fig. 2—Lesions around the mouth in Scalded Skin Syndrome.

There was no preceding lesion or history of drug ingestion. Purulent conjunctivitis was evident on the day of admission. On the second day, desquamation was seen on the face and neck, with associated flaccid bullae on the face and back. Erythema spread to the thighs on the second day. The child continued to be febrile and irritable, but could feed well. On the third day, desquamation was seen in the axillae, arms, face and neck. Denuded areas appeared with peeling of the skin and Nikolsky Sign was strongly positive.

Laboratory investigations revealed a hemoglobin of 13 gm%; the total leucocyte count was 19,400/cu.mm. with neutrophils 50%, lymphocytes 46%, monocytes 2% and eosinophils 2%. Urinalysis was normal. Cultures from the right ear, both eyes, nasopharynx and skin grew coagulase positive staphylococci (group II, phage type 3A/3C/55/71).

Blood and spinal fluid cultures were negative. Quantitative estimation of immunoglobulins showed normal IgG and IgM but the IgA level was low, 25 mg% versus an expected normal value between 46-400 mg%.

Therapy was started on the day of admission with saline soaks to the skin and frequent eye and mouth washes. Fluids were given orally in a volume of 2400 ml/m^2/day. Methicillin 200 mg/kg/day was given intravenously and later changed to oxacillin orally for a total duration of 10 days. Improvement was noted within a day and on the third day of admission, (fifth day after onset), he became afebrile. By this time, his skin had started healing and the Nikolsky Sign had become negative. Complete healing occurred in eight days.

Discussion

The exact incidence of 'scalded skin syndrome' associated with staphylococcal infection is not known. Constantino et al.[5] reported three cases, two due to staphylococci and collected 10 from the American literature. Tyson and colleagues[6] reported three cases, two due to staphylococci. Lowney et al.[7] reported 10 cases, two associated with coagulase positive staphylococci. Lyell, Dick and Alexander[8] reported six cases due to coagulase positive staphylococci and Melish and Glasgow[4] discuss 28 cases.

Clinical Manifestations

The clinical manifestations vary and include at least three principal modes of presentation.

Exfoliating Dermatitis

The most common picture is of a child who has a rather abrupt onset of widespread erythema, marked tenderness of the skin with a dry, coarse, "sandpaper" texture. This is soon followed by separation of the epidermis so that after light stroking, the epidermis becomes wrinkled, producing a positive Nikolsky Sign (Figure 3). Flaccid bullae then form followed by separation of



Fig. 3—Positive Nikolsky sign and pustular lesions on the abdomen.



Fig. 4—Peeling of skin in large sheets.



Fig. 5—Note the lesions around the mouth and face. Desquamated lesions were also present on the neck and shoulders. The right anticubital fossa has a denuded, red moist area due to peeling of the skin.

large sheets of the epidermis leaving moist re raw areas behind (Figure 4). These areas dry i about two days. Thick dry flakes appear on thes areas, characteristically around the mouth. Th thick yellowish dry patches separated by red de nuded fissures around the mouth form a charac teristic appearance which was present in all ou cases (Figure 5).

Complete healing without scar formation us ually occurs in eight to 10 days.

Scarlatiniform Rash

The second picture is a generalized scarlatini form erythema, "sandpaper" skin texture and dif fuse tenderness of the skin. In the next two t three days, the erythematous areas become dry thickened and cracked and the skin desquamate in large dry flakes especially around the mouth In the early stages and the final desquamativ stages, the first and second presentations are alike However, this picture is characterized by the ab sence of the intermediate stages of bullae forma tion and widespread exfoliation. This can be dif ferentiated from Streptococcal Scarlet fever by th absence of 'Strawberry tongue,' enantham or posi tive streptococcal culture.

Bullous Impetigo

The third mode of presentation, usually in the newborns is localized bullous impetigo. The same phage group II staphylococci are seen in these pa tients. None of our patients belonged to this group.

Other Presentations

A purulent staphylococcal conjunctivitis ap peared in the eary stages in approximately half of our patients and in several of the patients of Melish and Glasgow.[3,4] The syndrome may be preceded by impetigo or a secondarily infected skin. We observed infection of the throat and nose preceding the syndrome in half of our cases.

The course of the disease is variable. Although it may be fatal in the newborn infant, with proper fluid and electrolyte therapy, the prognosis is good. In the majority of cases, the recovery is complete within one to two weeks. Mortality rate of 0-7% has been recorded between one and five years of age, in contrast to an overall mortality of 23-30%.[7,9-12] The mortality is usually due to secondary infections and loss of fluids, protcins and electrolytes from the denuded areas. All our patients survived with complete healing within one to two weeks.

Pathology

The primary pathological lesion is epidermal necrosis with intra epidermal split at the level of the stratum granulosum. Occasionally, detachment of the epidermis at the dermal-epidermal junction is seen. No inflammatory reaction occurs in either the epidermis or the dermis. Many investigators have reported an association of the entity with group II staphylococci especially with phage type 71 staphylococci.[6-8,10,13-16] The work of Melish and Glasgow[3,4] has given a conclusive proof to this association. They found association of group II coagulase-positive staphylococci in all the 28 children presenting with the scalded skin syndrome. The staphylococci isolated from these patients produced exfoliation in newborn mice. Typical skin reaction was produced in mice by intraperitoneal injection of these organisms, whereas, staphylococci belonging to phage type other than group II failed to evoke a similar reaction. The lesions progressed from the development of a Nikolsky Sign to bullous formation and exfoliation. The staphylococci could be recovered from the involved animals, thus fulfilling Koch's postulates. The clinical picture, sterile bullae and lack of inflammatory reaction in epidermis or dermis suggests that the skin reaction is due to some soluble substance produced by group II staphylococci. This is supported by the experimental observations of Melish and Glasgow[3] that focal intraperitoneal inoculation of group II staphylococci in newborn mice evoked generalized widespread skin reaction typical of scalded skin syndrome. In nine of our patients, coagulase positive staphylococci were cultured from multiple sites including the throat in seven. Staphylococci were also cultured from the eyes in three of the six children in whom cultures from the eyes were obtained. These observations strongly suggest that the eyes and nasopharynx could be the source of infection at least in some patients. It seems very likely, therefore, that staphylococci group II produce some substance which disseminated from a focal site of infection to produce widespread dermal erythema, tenderness, bullae and exfoliation.

Several 'toxins' formed by group II staphylococci have been studied. The substance or toxin related to scalded skin syndrome has been found by Melish, Glasgow and Turner[17] to be a macromolecular ampholyte with some characteristics of delta hemolysin. It was found to be distinct from alpha and delta toxins by Kapral and Miller[18] who named the factor "Exfoliatin" because of its epidermal splitting activity. Arbuthnott, et al.[19] have also confirmed the presence of a separate "epidermolytic toxin" which is distinct and separate from hemolysin.

Therapy

A vigorous supportive care similar to burn therapy is necessary since fluid, electrolyte and protein loss from the denuded skin may be quite marked. Repeated evaluation of the level of hydration, electrolytes and proteins is mandatory so that necessary replacements may be made. Most of our patients could maintain an adequate oral intake in spite of severe lesions around the mouth and on other parts of the skin. Skin care includes isolation to avoid secondary infection and normal saline soakings. Eyes and oral mucosa need repeated washing.

After obtaining appropriate cultures from skin, eyes, pharynx and blood, the children should be given antistaphylococcal therapy. We have used methicillin in doses of 200 mg/kg/day I.V. initially. This is changed to oral oxacillin after clinical improvement is apparent. Steroid therapy has been advocated by some authors (Constantino, et al.)[5] and condemned by others (Melish and Glasgow).[4] Considering the association of the condition with staphylococci, we feel quite strongly that steroids have no place in the therapy of these patients.

Summary

Thirteen cases of toxic epidermal necrolysis are presented. Eleven of the 13 cases were associated with coagulase positive staphylococci. Phage typing was done in four and it revealed group II phage types 55 and 71. The disease may manifest as exfoliating dermatitis, scarlatiniform rash or bullous impetigo. Conjunctivitis is often present. Staphylococci were cultured from the nasopharynx in seven of our cases. All the patients recovered without sequelae. The syndrome is most likely caused by a specific exfoliative toxin liberated by group II staphylococci.

Acknowledgments

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Before the Doctor Arrives

ARTHUR F. GIERE, Ph.D., D.JUR.

IN THE YEAR 1891, a medical doctor named Fredrik Mohn, published a book in the Norwegian language, entitled, "Before The Doctor Arrives," which contained much information about medical aids and health directions. This book was printed in Decorah, Iowa, and contained 151 pages.

This volume is very interesting since it recorded the thinking of the medical profession which existed 79 years ago. It is also a noteworthy item of Norwegian-American history. Here is a free translation of some of the interesting bits of the medical specifications and health regulations designated in this book. The Physician writes:

"When ought a man to marry? It would be best when he is one or two years older than the girl.

"Never visit a sick person when you have an empty stomach. That is a rule which never must be violated.

"When a sick person dies the body must be immediately placed in a coffin which has been tarred on the inside and made airtight and then it must be promptly removed from the room.

"Women must get rid of their corsets, because so many illnesses are caused by the use of corsets. The circulation of the blood is stifled and numerous women have become weak and unhealthy. So, for God's sake throw away the corsets.

"Whom should a Norwegian marry? I would recommend that all Norwegians marry people o German extraction. The dyspeptic Americans and the flat bosomed American women and all maidens who are so dumb that they want to act like the Yankees, in this matter, are not very attractive nor desirable as mates, so it should not be necessary to advise people not to get married to any of them.

"Women's under pants should always be of wool and should reach to the ankles instead of only to the knees and in the wintertime, all women ought to wear two pairs of pants, both reaching to the ankles.

"What should one do to reduce weight? Fat people who wish to become lean should never eat more than five ounces of meat or fish for breakfast together with a large cup of tea, without sugar or milk, and an ounce of bread and a soft boiled egg. For the noon meal, one may eat six ounces of any kind of fish or meat, except herring or pork or veal. One should eat greens, but no potatoes, nor beets nor carrots. One can have one ounce of dry toast, some fruit pudding and a glass of wine. Champagne, beer or port are, strictly, forbidden. For the evening meal, three or four ounces of the above named fish or meat and a small cup of tea with toast and three ounces of fruit. All fat persons should have physical exercises and take daily walks."

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Spontaneous Cholesterol Embolic Renal Failure

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RAPIDLY PROGRESSIVE RENAL failure in the elderly is a common and extremely serious medical event. When renal failure is complicated by the rapid onset of hypertension with oliguria or anuria, the diagnosis of cholesterol embolization to the kidneys should strongly be entertained.[1-8]

Case Reports

Case 1

A 72-year-old male was well until December 21, 1967 when he underwent surgery for a ruptured abdominal aortic aneurysm below the renal arteries. Both common iliac arteries were involved in the aneurysm. A Y-shaped Dacron graft was inserted. The resected specimen contained many cholesterol crystals. Postoperatively, the femoral pulses were strong and the urine output was adequate, but the blood urea nitrogen rose from 26 mg% preoperatively to 81 mg% on the fifth day. Intravenous pyelogram showed good excretion in a normal left collecting system, but only a nephrogram on the right. Cystoscopy and a right retrograde pyelogram were normal. The blood urea nitrogen subsequently fell to 25 mg% by the time of discharge from the hospital.

He was again hospitalized in 1970 for transient cerebral ischemic attacks. Electroencephalogram, lumbar puncture and brain scan were normal. He was treated with oral anticoagulants and was discharged much improved.

The third admission, for congestive heart failure, came in May 1971. He responded rapidly to digitalis and diuretics. His blood urea nitrogen was 41 mg%, creatinine clearance 33.5 cc/minute and a urine culture was negative.

His final admission was in July, 1971 when he developed thrombophlebitis of the right calf and popliteal area. The blood pressure was 200/120; and fresh flame-shaped hemorrhages were noted in both fundi. In addi-

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Fig. 1—(Patient No. 1) Abdominal aorta. Atheromatous plaque showing cholesterol crystals. (Hematoxylin and eosin; original magnification x 100).

tion he had moist rales at both bases posteriorly, an S_3 gallop and left ventricular heave. Admission blood urea nitrogen was 63 mg%; chest film revealed mild congestive heart failure and left ventricular prominence. Electrocardiogram revealed an old anterior myocardial infarction.

Hospital Course: Parenteral administration of α-methyl Dopa was begun with a prompt drop of the blood pressure to 110/80. The patient did well until July 24 when he left the hospital on a weekend pass. He returned feeling worse with a weight gain of 2.7 Kg. By the next morning, he developed chills, fever, diarrhea and mental confusion. Medications were stopped. Two days later, the blood urea nitrogen rose to 85 mg%, the serum creatinine to 9.5 mg%. Urine culture grew Klebsiella; gentamycin was started in doses appropriate to the serum creatinine. On July 26, blotchy livedo reticularis and petechiae appeared from the lower abdomen down to the feet. Simultaneously urine output dropped from 400 cc/day on July 26 to 140 cc/day on July 30, in spite of adequate blood pressure and large dose of intravenous furosemide. The livedo reticularis and petechiae waxed and waned for the next two days. Repeated blood cultures were negative. Biopsy of several petechial lesions failed to show either bacterial clumps or cholesterol clefts. On August 2, a left retrograde pyelogram showed no obstruction. A translumbar aortogram showed intact renal arteries and poor renograms. On August 4 and August 5, the patient underwent hemodialysis for four hours each day. The blood urea nitrogen dropped to 66 mg% and the serum creatinine to 6.9 mg%. His sensorium deteriorated and the livedo reticularis of the lower extremities worsened. Urine output declined and the blood urea nitrogen rose to 171 mg%. The patient died on August 25.

Autopsy: The prosthetic abdominal aortic graft was in good condition, but there was aneurysmal dilatation of the aorta above the graft. Microscopic sections of the aorta showed severe atherosclerotic destruction and mural thrombosis. Most of the thrombi were old and hyalinized and contained innumerable empty, cholesterol crystal clefts with no inflammatory reaction. Both kidneys showed varying degrees of tubular atrophy in wedge-shaped areas. There was only mild to moderate arteriosclerosis of the renal arteries but there were multiple clusters of empty cholesterol crystal spaces, usually surrounded by multi-nucleated giant cells and a small amount of loose connective tissue occluding the vessels. The atrophic cortical areas did not suggest old necrotic infarcts but appeared to be the result of a slower atrophic process (Figures 1 and 2).

Occlusion of medium sized arterial branches by cholesterol emboli were also found in the spleen, adrenals, pancreas, testis and vertebral bone marrow.

Case 2

A 79-year-old white male entered the hospital on June 29, 1971 because of symptoms of congestive heart failure. Physical examination revealed an oriented, mentally competent, elderly male in no acute distress. Pulse was 100, the blood pressure 170/105. The neck veins were distended at 60° elevation and basilar moist rales were audible posteriorly. The cardiac rhythm was regular and an S_4 gallop was present. There were multiple surgical scars on the abdomen and the liver was palpable 2 cm below the right costal margin. There were no abdominal bruits. Pitting edema was present in both lower extremities to the knees.

The past history included a sigmoid colectomy for diverticulitis, a partial gastrectomy for chronic peptic ulcer disease and a cholecystectomy. In 1965 he had a transurethral resection of the prostate for benign prostatic hypertrophy. In 1966 he was treated for a urinary tract infection, after which his blood urea nitrogen was 18 mg%, the serum creatinine 1.3 mg%. The blood urea nitrogen in April, 1971 was 20 mg%, rising to 32 mg% later that month. Urinalysis and culture were negative at that time. Intravenous pyelogram showed both kidneys to be 10 cm long; the left kidney showed poor function

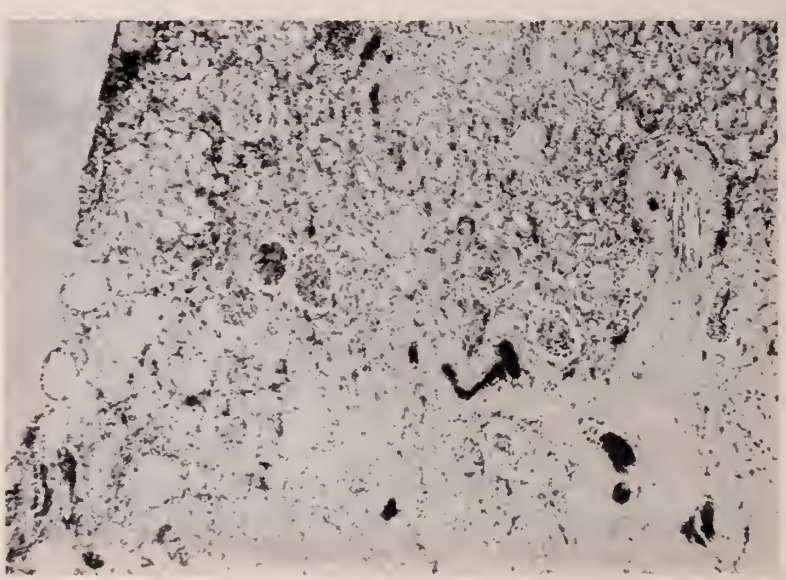


Fig. 2—(Patient No. 1.) Renal cortex. Cholesterol crystals in an arteriole with adjacent parenchymal atrophy. (Hematoxylin and eosin; original magnification x 450).

and the collecting system did not visualize well.

On admission (June, 1971) the blood urea nitrogen was 33 mg%, the serum creatinine 3.7 mg%; urinalysis showed 21-30 white blood cells per high power field, 1+ proteinuria, and no casts. Urine culture grew greater than 10^6 colonies of Enterococcus. The chest film revealed mild congestive heart failure. Electrocardiogram showed left axis deviation and an old anteroseptal myocardial infarction. The patient was treated with digitalis and diuretics and he improved rapidly. On July 6 he had a sudden rise of temperature to 105° F. and became obtunded. The blood urea nitrogen was 51 mg%, the serum creatinine 5.2 mg%. Urine culture again grew greater than 10^6 Enterococci. Blood, cerebrospinal fluid and sputum cultures revealed no growth. Urine output fell to 150 cc/24 hours. Cerebral echogram showed a 1-2 mm shift of the pineal from left to right. Brain scan showed increased activity over the left convexity, possibly consistent with infarction or other early injury in the left Sylvian area. Repeat lumbar puncture, brain scan and electroencephalogram were not diagnostic. He remained comatose for the next four days, while the fever declined gradually. Urine cultures then revealed no growth. Over the next ten days, his sensorium slowly cleared and the urine output increased temporarily. In spite of urine output in excess of 1000 cc/24 hours, the azotemia worsened, the patient again became comatose and expired on August 26, 1971. The last blood urea nitrogen was 110 mg% and his urine output for the last 24 hours was 225 cc.

Autopsy: Bilateral bronchopneumonia and severe atherosclerosis of the aorta with some "egg shell" calcification and ulcerations of the intima were found. Microscopically, many of the mural thrombi were extensively hyalinized and many of these contained innumerable empty cholesteral crystal clefts without inflammatory reaction. Examination of the kidneys revealed no evidence of active pyelonephritis and there was only moderate arteriosclerosis of large and medium sized arteries. The striking finding was the occlusion of many medium sized and small renal arteries by clumps of cholesterol crystals. These occluded vessels were related to wedge-shaped areas of renal tubular atrophy in the adjacent cortex. Similar small artery cholesterol emboli were found in sections of the spleen, pancreas, testes and in the small mucosal arteries of the small intestine.

Discussion

Clinical Setting and Pathogenesis

Atheromatous emboli occur in two principal forms, the first is the so-called atheroembolus. This form of embolization occurs when large plaques are dislodged from their origin and occlude major arterial branches downstream. Recognition of this problem is seldom difficult because of the very dramatic and often catastrophic nature of the embolic event. The second form, the so-called cholesterol embolus is subtle and difficult to recognize. Cholesterol emboli occur when cholesterol crystals and other atheromatous components are released or dislodged from erosions of atheromatous plaques.

The embolized particles are microscopic in size, and unless the occlusion involves strategically important blood vessels, the entire event may remain silent.

The usual clinical setting of cholesterol embolization is a procedure involving the abdominal aorta. Thus embolization is frequently preceded by aortography with contrast studies. The relatively stiff catheter is often lodged into an area of erosion on an atheromatous plaque, and the injection of contrast material under high pressure may produce showers of emboli downstream from the diseased area.[9] Surgical manipulation of a diseased aorta, especially at the time of replacement of an abdominal aortic aneurysm with a prosthetic graft may easily fragment atheromatous plaques and cause emboli.[3,10] In this latter setting, due to the proximity of the renal arteries to the operative field, the kidneys often become the site of cholesterol embolization which may lead in the immediate postoperative period to anuria or oliguria.

Cholesterol emboli may also occur spontaneously, most likely from bleeding into an eroded atheromatous plaque with dislodgement of cholesterol crystals.[5,6]

Although the abdominal aorta is perhaps the most common source of cholesterol emboli, other vessels have been noted to give rise to similar events, especially the ascending aorta in syphilitic patients, the coronaries, and the proximal internal carotids.[2,11]

Pathology

The lodgement of cholesterol emboli are seen as long needle-like slits in the medium and small arteries (150-200 μ in diameter),[5] which stimulate a foreign body giant cell reaction. Following the initial insult, fibroblasts proliferate about the crystals and the giant cells disappear after a variable period of time. The vessels may then recanalize, re-establishing some patency to the lumen. The end result of this process is a fibrosing endarteritis with marked reduction in the caliber of the blood vessels.[2,4,5,12]

Renal Involvement

The kidney is the organ most frequently involved in this process. The fibrosing endarteritis occurs in the smaller renal vessels causing tissue ischemia distal to the occlusion. This in turn leads

to dysfunction, atrophy and rarely to necrosis. In the kidney the majority of the ischemic changes are seen in the renal cortex, and the extent of renal damage is well correlated with the magnitude of the occlusive process. The occlusive lesions are frequently found at bifurcations of arteries. Arcuate, intralobular, and terminal arteries are most frequently affected. Multiple occlusions can account for the patchy ischemic degeneration of the renal cortices. Spotty cortical atrophy, usually wedge-shaped is the major finding. The wedge-shaped zones of ischemia are interspersed between relatively normal renal tissue, and frank necrosis is rarely found.[2,6,7,13] The hypertension that often follows cholesterol emboli to the kidneys is most likely mediated through the renin-angiotensin-aldosterone mechanism.[2,10] The location of the emboli proximal to the juxtaglomerular apparatus further adds validity to this theory.[10] The hypertension can be a new finding with an abrupt rise of previously normal blood pressure or on occasion, intensification of existing moderate hypertension.[4,6,7,9,12]

The other major renal complication of cholesterol emboli is renal failure which may manifest itself as acute oliguria or anuria. Rarely, urine output remains normal in the face of rising creatinine.[3,4,7,10] The renal failure occasionally occurs in a step-wise progressive fashion temporally related to episodes of showerlike embolization.[4,7]

Clinical Manifestations

The usual manifestations of cholesterol embolization will largely depend on the site and extent of the embolic process. Frequently, there are no readily recognizable signs or symptoms because of the spotty involvement of the affected organ and because of the presence of adequate collateral circulation. Since the abdominal aorta is the usual site of origin for these cholesterol emboli, the abdominal viscera are most frequently involved. The kidney, pancreas and spleen are the organs most frequently involved.[2,10,14]

In addition to visceral involvement, cholesterol embolization may be manifest by ischemic changes of the lower extremities with pain, livedo reticularis, cyanosis, and gangrene despite adequate arterial pulses, showers of petechiae on the lower extremities and abdominal wall and subcutaneous nodules.[12] Occasionally, abdominal pain, gastrointestinal hemorrhage and pancreatitis may overshadow these complaints.[2,4,6,15] When the source of the cholesterol emboli is in the ascending aorta, especially in an aorta diseased by syphilis, the main findings may be neurological, with transient blindness due to embolization to the retinal vessels and/or various cardiovascular complications.[2,11]

The clinical diagnosis is difficult in these patients. There are no distinguishing characteristics of this form of oliguric renal failure from any other in the older age group. Examination of the urinary sediment is nonspecific; there is modest proteinuria, and a slight increase in red and white blood cells, with occasional hyaline and granular casts.

The definitive diagnosis of cholesterol emboli can only be made after histopathologic examination of involved tissues confirms the presence of cholesterol clefts. In the first patient, the diagnosis was suspected because of the recurrent showers of petechiae in the presence of rapidly progressing hypertension; however, the histopathologic examination of one of the excised petechiae failed to show the expected cholesterol crystals. In the second patient the diagnosis was not considered antemortem.

In the clinical setting of rapidly advancing hypertension with or without oliguric renal failure every effort should be made to establish the correct etiologic diagnosis. Separation of cholesterol embolization from other clinically similar conditions is important in that the various forms of vasculidities, such as polyarteritis nodosa or subacute bacterial endocarditis may be treated with specific therapy, while cholesterol emboli at the present time may be treated symptomatically only.

It is of further interest to note that the first patient was on long-term oral anticoagulant therapy for transient ischemic attacks just prior to the clinical onset of cholesterol embolization. Moldveen-Gerominus and Merriam pointed out that anticoagulation may enhance cholesterol embolization by preventing adequate thrombus formation over an eroded atheromatous plaque.[14]

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3-15 See page 1104.

Bilateral Hip Arthroplasty after Renal Transplantation

Total Rehabilitation of the Patient

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RENAL TRANSPLANTATION has now moved from the realm of the experimental into that of practical therapeutics. Experience at the Mayo Clinic with more than 120 renal allografts shows a rate of rehabilitation with successful transplants of 90% or higher, despite the fact that transplantation is being offered to patients previously excluded as extremely high risks. In the following case the details of total rehabilitation in a patient with the double handicap of end-stage renal disease and bilateral avascular hip necrosis are reported.

Report of Case

A 37-year-old man was first seen at the Mayo Clinic on Jan. 13, 1969, with end-stage renal disease. In 1953 he had been rejected for military service because of proteinuria. He felt well, however, until gross hematuria occurred in 1958. At this time, a diagnosis of chronic nephritis was made and a protein-restricted diet was begun. He did well on this regimen until June 1968, when numbness developed in the toes of both feet and paresthesias developed in the first three digits of both hands. Because of increasing renal failure and hypertension, the dietary intake was reduced to 18 gm of high biological value protein and 40 mEq sodium and treatment with alpha methyldopa was started. Although the neurologic symptoms abated somewhat, the patient was referred by his family physician to the Mayo Clinic to be considered for renal transplantation.

Physical Examination

On physical examination, the blood pressure was 160 mm Hg systolic and 100 mm Hg diastolic. Uremic fetor was present. In the upper extremities, vibratory sensation was decreased. In the lower extremities deep tendon reflexes were hypoactive and associated with hyperesthesia of the soles, moderate decrease in vibratory sensation, and moderate pretibial edema.

Laboratory Studies

Laboratory studies included urinalysis with specific gravity of 1.005, pH—6.2, sugar—negative, and protein —grade 2; microscopic examination showed leukocytes, grade 1, with occasional hyaline and granular casts. The leukocyte count was 9,400 and the hematocrit reading was 34%. The value for serum creatinine was 18.8 mg/100 ml, for calcium, 8.7 mg/100 ml, and for phosphorus, 10.2 mg/100 ml.

Urologic and Psychiatric Evaluations

Urologic and psychiatric evaluations did not reveal contraindication to surgery. After an appropriate evaluation and tissue typing, the patient's sister was accepted as a kidney donor. Accordingly, on January 29, 1969, bilateral nephrectomy and renal transplantation were accomplished without incident. Pathologic examination of the patient's kidneys revealed chronic glomerulonephritis. The serum creatinine fell from a preoperative value of 20.5 mg/100 ml to 1.1 mg 11 days later.

The patient was dismissed from the hospital in February, 1969. Ten days later his serum creatinine measured 2.75 mg/100 ml and the amount of prednisone was increased from 50 mg/day to 100 mg daily for several days and maintenance therapy with azathioprine (Imuran) (2 mg/kg) was continued with a resultant gradual return of serum creatinine to the previous normal level. Oral doses of prednisone were gradually reduced over the subsequent months to a level of 20 mg daily by October 27, 1969.

Two months later the patient complained of pain in both hips and roentgenograms revealed evidence of bilateral avascular necrosis. Nonweight-bearing crutch-walking was instituted and the patient remained ambulatory and active for several months, spending long hours driving a tractor without major problems. Follow-up roentgenograms, however, revealed evidence of continued progression of hip necrosis, so that by January, bilateral total hip arthroplasty was deemed necessary. Renal function continued at normal levels with the serum creatinine at 1.0 mg/100 ml.

On January 6, 1971, after steroid preparation with 200 mg of cortisone acetate given intramuscularly before operation (repeated on the day of surgery and the following day), left total hip arthroplasty was performed with insertion of a stainless steel Charnley prosthesis. Sixteen days later the procedure was duplicated on the right hip. Immunosuppression was maintained at preoperative levels of azathioprine (2 mg/kg/day) and prednisone 12.5 mg/day). Recovery was uneventful except for a temporary moderate rise in serum creatinine,

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which promptly returned to normal levels after four consecutive days of treatment with intravenous injections of methylprednisolone (1 gm/day).

Within three months the patient was walking normally without support. Over the ensuing months he returned to farming, including the lifting of 29.5-kg bales of hay. In addition, he started working 40 hours a week in a factory, so that by September 1971, he was working 90 hours per week regularly. He has continued this workload until the time of this report, 38 months after renal transplantation. The serum creatinine value remains at 1.15 mg/100 ml. The patient takes a maintenance dosage of prednisone—10 and 7.5 mg on alternating days—and a daily dose of 150 mg of azathioprine. His health is excellent except for continuing mild hypertension (160/100 mm Hg).

Comment

This case illustrates full rehabilitation of a patient after treatment for two severely disabling disorders. The avascular necrosis was no doubt secondary to relatively high doses of steroids ingested for several months after a rejection episode. Recently, we have substituted intravenous injection of methylprednisolone for oral doses of steroids in the treatment of rejection, avoiding more than 25 mg of prednisone per day by mouth.[1] This change has resulted in a rather low incidence of avascular necrosis (1.5%—1 of 67) as compared to our previous experience (9%—5 of 53) in patients receiving higher oral doses of prednisone.[2] The magnitude of the operation necessary to correct this condition and the patient's surprising tolerance are indications of the resilience we have noted in the majority of patients whose transplants are successful. This patient's involvement in heavy physical labor likewise attests to the capacity of such patients to lead a normal life.

The most important single factor in rehabilitation, in our opinion, however, is motivation. In our experience the patient who is positively oriented toward specific goals inevitably performs superiorly. It is our impression that one of the prime considerations in acceptance of a patient as a potential transplant recipient should be a strong desire to return to a productive and normal life in his community. The present patient is illustrative of such an outlook.

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And he gave it for his opinion, that whoever could make two ears of corn, or two blades of grass, to grow upon a spot of ground where only one grew before, would deserve better of mankind and do more essential service to his country, than the whole race of politicians put together.*

*Swift: Gulliver's Travels.

Cerebral Schistosomiasis

A Report of 10 Cases Caused by Schistosomiasis Japonica

THOMAS A. HAEDICKE, COLONEL, USAR (MC)

THE FIRST RECORDED evidence of central nervous system involvement by Schistosoma japonicum was published in 1906.[7] In that year Tsunoda and Shimamura[7] described a case which was characterized by a right-sided hemiplegia and Jacksonian convulsions. Many ova of Schistosoma japonicum were demonstrated at autopsy in the cortex, choroid plexus, basal ganglia and meninges.

The ova of Schistosoma japonicum always affect the brain, leaving the spinal cord untouched. The ova of Schistosoma haematobium[9] and Schistosoma mansoni,[6] on the other hand, affect primarily the spinal cord and only occasionally the brain.

Gama and De Sa[6] reported the first case of Schistosoma mansoni involving the spinal cord in 1945. Their case showed signs of spinal fluid block and the symptoms were typical of a flaccid paraplegia. Ova of Schistosoma mansoni were found in some pieces of tissue removed from the conus medullaris.

Kane and Most[4] observed 27 cases due to Schistosoma japonicum from October 20, 1944, to May 1, 1946. A clinical diagnosis was made on 22 of these cases. The remaining five were diagnosed from sections of tissue removed from the brain at operation.

Carroll[5] reported five cases in American troops that developed cerebral symptoms within seven months of exposure on the island of Leyte. Practically all of the American troops that developed this infection obtained it either from Leyte or from Mindanao in the Philippines.

Tsunoda and Shimamura[7] feel that the ova arrive by means of arterial embolism. Greenfield and Prichard[8] maintain that the female is lying within one of the cerebral sinuses and deposits her eggs in the smaller venous radicles entering the sinus. There are many other theories as to the route that is taken by the parasites, and they are well summarized by Speigel.[1] The mechanism of spread via the vertebral veins has not been mentioned previously, and it is felt that the involvement of the brain could be explained by ova traveling this route.

Many of the patients diagnosed as having cerebral schistosomiasis recovered without any treatment; Tillman[11] reported several that recovered

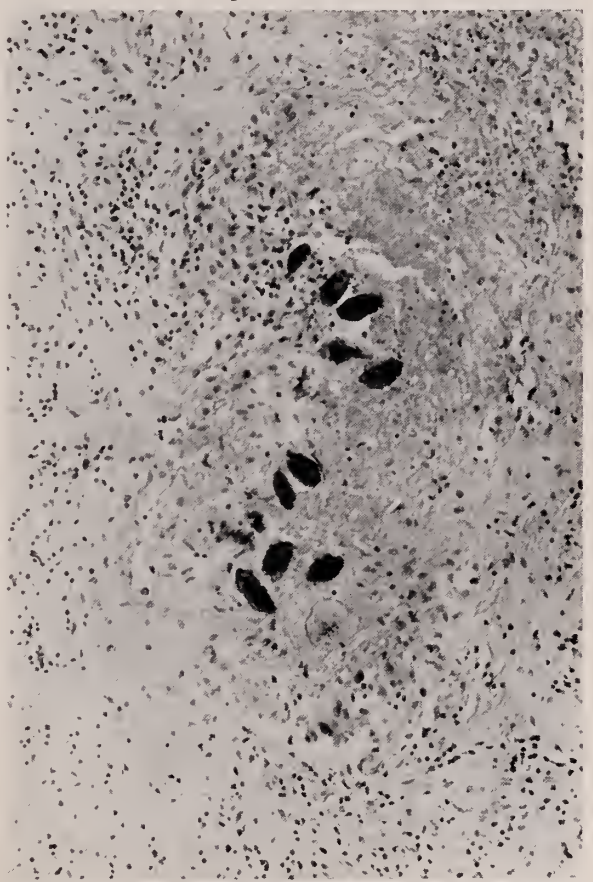


Fig.1—Section of brain showing parasites in cross-section. These measure 30-1000 micra in size, the shortest to the longest diameter. The outer layer is composed of a refractile chitinous layer. The parasites are located in the tubercles of necrotic material.

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from confusion, aphasia and hyperreflexia without any treatment.

A few cases were operated on because the diagnosis of cerebral schistosomiasis was not entertained, or because it was felt that a operation would alleviate some of the symptoms. Watson, Murphey and Little[3] reported a case that was operated on after a ventriculogram showed a large expanding lesion in the left parietotemporal region. It was necessary to perform a second craniotomy four months later because the seizures were uncontrolled on large doses of dilantin and phenobarbital.

Faust and Meleny[10] have given us an excellent monograph on schistosomiasis which covers the involvement of the central nervous system. The most important symptoms that these patients have are hemianesthesia, visual field defects, hemiplegia, headaches, paresthesias, unconsciousness and epileptiform seizures. When any of the above symptoms appear and the patient has a history of schistosomiasis, Cutler[2] recommends the institution of early treatment in selected cases, regardless of the fact that ova cannot be demonstrated in stools.

The ten patients in this report developed their infection on the islands of Leyte and Mindanao in the Philippines.

Case 1

A 28-year-old white male was in a combat engineer group engaged primarily in bridge building under fire. In December of 1944, while on Leyte, he spent most of his time working in the water.

Exposure

The men engaged in bridge building had been warned to stay out of water as much as possible because of the possibility of schistosomiasis in that areas.

Early Symptoms

During that time he developed red spots and itching on his forearm. Approximately one week after the skin lesions became evident he had diarrhea for one day consisting of five to six fairly loose stools. In February of 1945 he was sent to the hospital for a 10-day periodic check up. Prior to going he had an elevated white count. Several stool examinations were performed, none of which showed any evidence of schistosomiasis. He was then returned to duty with the recommendation that stools be examined again in one month. One month later enroute to Okinawa he developed severe headaches, nausea, vomiting, anorexia and marked weakness. Gradual improvement was noted following bed rest, but on his arrival at Okinawa in April 1945, he had further frontal headaches and dizziness, which increased in severity.

Localizing Symptom

On 1 May it was found that he could not focus his eyes. He had three episodes of rather severe objective vertigo, each one two minutes in duration, during which his entire body felt as if it were rotating from right to left. The headaches gradually became more violent and he was placed in quarters. During this time he began to vomit and felt as if he would have to vomit each time he changed his position in bed. He did not improve on outpatient treatment and was evacuated to an Army General Hospital in the United States on 11 June 1945.

Physical Findings

Examination at that hospital showed bilateral choked discs, hyperactive reflexes everywhere, complete left homonymous hemianopsia and a left positive Hoffman's sign. A *ventriculogram* showed a shift of the ventricles, including the third ventricle, to the left with deformity of the right lateral ventricle. This deformity suggested a mass pressing upon the ventricles from above and laterally. A small amount of material taken through a needle showed inflammatory tissue containing numerous eosinophils. On 12 July the patient had a left-sided generalized convulsive seizure associated with paresthesia of the left half of the body.

Results of Operation

He was operated on 16 July; a mass 3 cm. in diameter was removed from the right occipital lobe, and he had an unremarkable postoperative course. There were no seizures following the operation. He showed some incoordination and unsteady gait during the first month, but this gait improved and became satisfactory. He had a mild persistent left homonymous hemianopsia and a mild

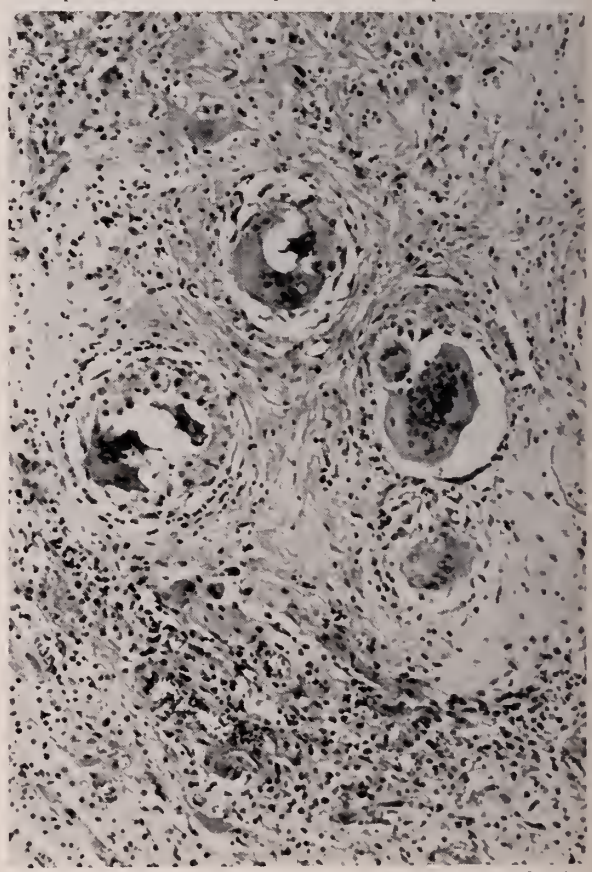


Fig. 2—Section of brain showing parasites engulfed by giant cells within the tubercle.

central type of left facial weakness with some mild weakness of the left fifth and ninth nerves. Electroencephalograms showed only a small-focus low wave arising in the right parieto-occipital region. White blood counts were within normal limits. Eosinophile counts were 5% to 9%. His white count prior to the operation had shown 10% to 12% eosinophils.

Pathology

Microscopic sections revealed no architectural outline. The sections were composed of numerous, small, round cells with colorless cytoplasm; there were also larger cells with abundant pink cytoplasm, suggestive of epithelioid cells. In addition, there were many eosinophils present and a suggestion of epithelial arrangement around some blood vessels. Pathological diagnosis: Inflammation, granulomatous, suggestive of schistosomiasis. (Figures 1 and 2).

This patient was undoubtedly exposed to infection on several occasions since he was a combat engineer. The elevated white count during his first hospitalization indicates that he had schistosomiasis at that time. He was treated with 1.8 grams of tartar emetic following the operation, and a three month follow-up showed great improvement.

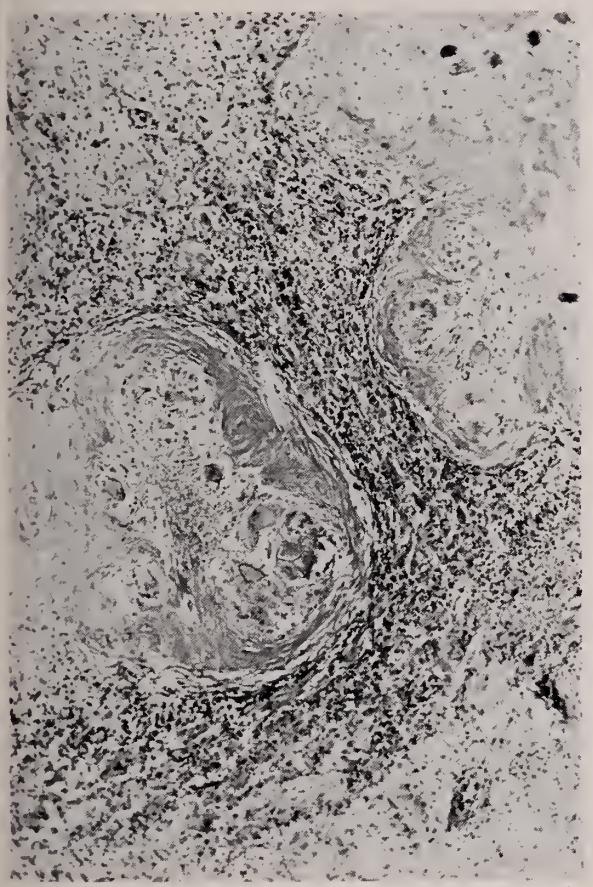


Fig. 3—In this section of brain marked lymphocytic and plasma cell infiltration can be seen ringing the tubercle. In the center of the tubercle can be seen cysts with refractile walls.

Case 2

Exposure

A 29-year-old while male, who was assigned to the Engineers building bridges on the Island of Leyte, was exposed to fresh water containing cercariae of Schistosoma japonicum.

Early Symptoms

At that time there was an onset of severe frontal headaches not related to time of day or activity, and not relieved by aspirin or codeine but by morphine and pantopon. Approximately one month after the headaches had started, they occurred more frequently and persisted throughout most of the day. About two months after their onset the patient began having generalized convulsive seizures. His headaches continued through the six months prior to admission to Walter Reed Army Hospital, and three convulsive seizures occurred during that time. The past history was essentially negative; there was no family history of epilepsy or other mental diseases.

Physical Findings

Physical examination made in September 1945 was essentially negative, except for astereognosis of the left hand. Xrays of the skull, AP and lateral, were negative. *Ventriculography* showed ventricular shift to the left side with failure to fill the right posterior horn.

Results of Operation

In view of the convulsive seizures, the intensity of



Fig. 4—View of same section shown in Figure 3 under high power showing cysts with refractile walls within the area of granulomatous reaction.

pain associated with the headaches, the astereognosis of the left hand, and the ventricular shift to the left side, a right occipitoparietal bone flap was turned down. At this operation, a large nodular racemose type of tumor was found infiltrating the right occipitoparietal area.

Pathology

On gross examination portions of this tumor appear to be calcified. In the granulomatous area, the tubercles are both the hard and soft varieties; in the center of both tubercles, there is a cyst with a refractile wall; there is a marked lymphocytic and plasma cell ring around the tubercle. Pathological diagnosis of Schistosomiasis japonicum was made because of the size and occasional retained original configuration of the ova (Figures 3, 4 and 5).

This second patient became ill four months after his first exposure to water containing cerceriae of Schistosoma japonicum. The convulsive seizures he manifested were more severe than those found in epilepsy. His stools were positive for ova of Schistosoma japonicum following the operation. He was treated with tartar emetic 1.78 grams with complete relief of symptoms after a period of three months.

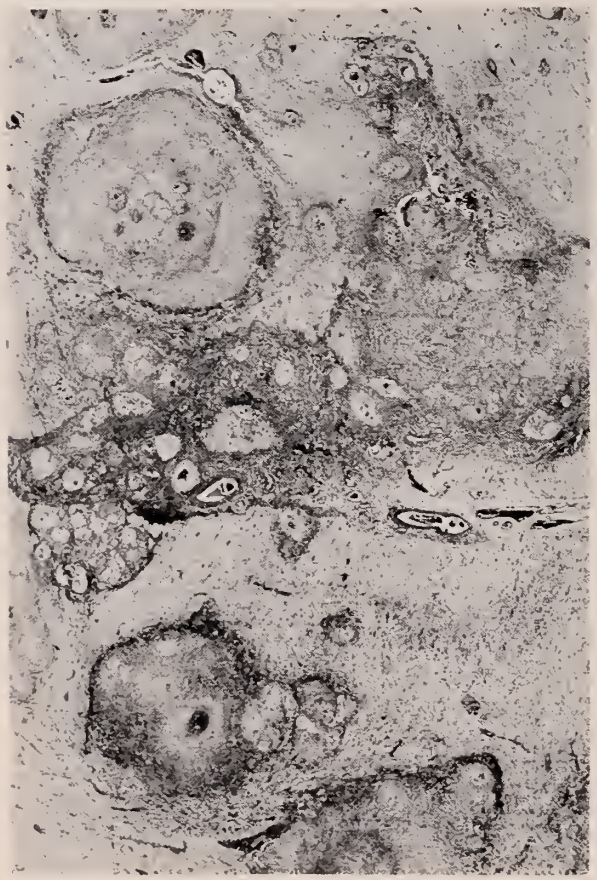


Fig. 5—Brain. Coalescence of tubercles is visible in this section.

Case 3

A 25-year-old white male became ill while on Leyte in October 1944 shortly after he began wading in fresh water streams there.

Early Symptoms

In January 1945 he had a severe nonproductive cough with vomiting and diarrhea. After leaving Leyte he went to Okinawa and felt perfectly well until May 1945 when he had a generalized convulsion. He was subsequently returned to duty. In June 1945 severe frontal headaches began and gradually increased in intensity. They were relieved with aspirin and codeine. In October 1945 the patient had another convulsion and also noted intermittent numbness of the right hand and increasing difficulty in writing. On 4 November 1945 he had a generalized convulsive seizure with trembling and twitching of the right side of the tongue and temperature of 96° to 102°. His speech was slurred and both optic discs were blurred. Laboratory studies revealed a leukocytosis with 11% eosinophilia. He was evacuated back to an Army General Hospital where a spinal fluid examination revealed 75 white cells, 90% polymorphonuclear, and a total protein of 100 mgm. percent.

Results of Operation

A craniotomy was performed on 13 December 1945 with a granulomatous tumor removed from the left

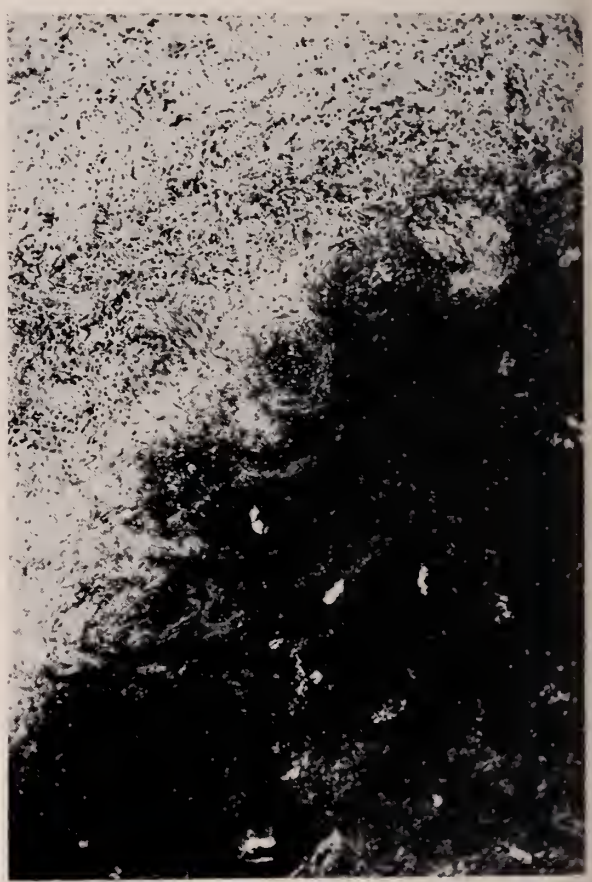


Fig. 6—Section of brain showing dense scar tissue made up of loose recently laid down mucoid collagen containing fibroblasts, plasma cells, numerous lymphocytes, neutrophiles, eosinophiles, and macrophages.

parietal cortex, which was subsequently shown to be due to Schistosoma japonicum with surrounding inflammatory reaction. He was then given a course of 75 cc. of fuadin intramuscularly. His stools were positive for Schistosoma japonicum ova. He was then placed on two dilantin tablets, 1½ grains each daily, following his operation. In March 1946 he was transferred to another Army General Hospital for more specific treatment. There he received a 30-day course of tartar emetic, and then had a follow-up of approximately 30 stools, all of which were negative.

Physical examination on admission to Walter Reed Army Hospital was essentially negative, except for a mild speech defect and weakness in the right hand. The reflexes were equal bilaterally, lungs and heart were normal, and the muscular system was essentially normal.

Laboratory findings in October 1946 revealed: Red blood count, 5,000,000 cells per cubic millimeter; hemoglobin, 98%; white blood count, 7,200 cells per cubic millimeter; neutrophils, 53%; lymphocytes, 43%; eosinophils, 4%. Sedimentation rate, 1. Wintrobe urinalysis, negative. Spinal fluid: Total proteins negative; cells—two lymphocytes. Six stool examinations were negative for Schistosoma japonicum ova.

This third patient continued to have generalized convulsions approximately once each month in spite of dilantin 300 mg. each day. His case is of particular interest because of his continued symptoms following the operation and treatment from fuadin and tartar emetic. He was discharged from the hospital on 600 mg. of dilantin a day. A three-month follow-up has shown that his symptoms are completely controlled.

Case 4

A 22-year-old white male whose present illness dates to 27 March 1945, while on Luzon, developed a generalized convulsive seizure followed by a violent headache of fifteen minutes' duration. The history disclosed prolonged difficulty with a left infraorbital abscess in 1926, at the age of four, which followed the removal of several teeth and was complicated by cellulitis, abscess, and osteomyelitis of the left side of the face. The patient had spent three years prior to this present illness in the Southwest Pacific, in Hawaii and the Philippine Islands. He bathed in the fresh water streams on Leyte, but he had no illness or any occasion to report to sick call during the entire three years in the Southwest Pacific. The day after his grand-mal seizure, he had an aura of bad taste, nystagmus with a rapid component to the left, and dilated pupils, a twisting of his head to the left, severe opisthotonos, severe cyanosis, and a major clonic seizure. Immediately after the seizure an examination revealed a positive Babinski on the right. An hour later, he again became unconscious for fifteen minutes, with a constant jerking of the right arm and leg. After that he had diplopia and constant severe headaches accentuated by turning, flexing and jarring the head. He walked with an unsteady gait, with a tendency to fall to the right, and his speech became slurred.

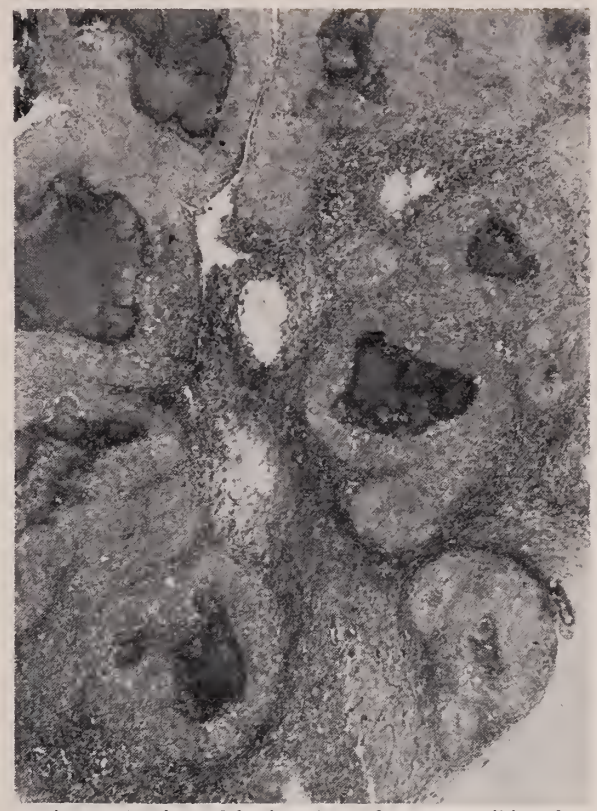


Fig. 7—Section of brain where the most striking feature in the mass of scar tissue was the broad geographic area of necrosis that resembled caseation necrosis.



Fig. 8—Brain. Many round cells present with colorless cytoplasm. An epithelial arrangement around some blood vessels is noted.

Physical Findings

Physical examination at this time showed bilateral, diminished corneal reflexes; bilateral sixth nerve palsy; papilledema of both retinae, more marked on the right; dysmetria, worse on the left; stiff neck; erratic response to pinprick, worse on the left; pupil dilated on the left; bilateral impaired hearing for high tone; and fanning of the toes bilaterally on plantar stimulation. An electroencephalogram revealed an irregular focus in the right anterior temporal region; a ventriculogram showed the lateral and third ventricles shifted to the left. In view of these findings and history, it was felt that the ventriculogram was positive evidence of a mass in the right frontotemporal area.

Results of Operation

An operation performed on 23 May 1945 revealed a hard, firm, dense mass in the right frontotemporal area, about the region of the Sylvian fissure. "The specimen consisted of a mass of firm, white tissue, measuring two cm. in diameter, and multiple additional fragments of firm, white tissue totaling 3 x 1 cm."

Pathology

Sections show that most of the tissue is composed of a dense scar made up of loose, recently laid down mucoid collagen containing many young fibroblasts, large masses of plasma cells, numerous lymphocytes, polys, eosinophils, and macrophages. In the necrotic areas, and especially in the macrophagic borders, there are found numerous parasitic forms. About three hundred of these were studied in numerous sections. The parasitic forms all have an irregular, thin, elastic-like, dense outer shell. Within the shell is a mass of pale protoplasm containing small, round, blue particles resembling lymphocytic nuclei. These parasites are typical of Schistosoma japonicum (Figures 6 and 7).

This fourth patient's illness was typical of the type manifested by many cases of cerebral schistosomiasis. The onset of a convulsive seizure was often sudden and without warning. His seizures were relieved by the operation, but there is no extensive follow-up on his ultimate course.

Case 5

A 27-year-old white male began to have left frontal headaches, blurring of vision and dizziness on 15 November 1945 while on the island of Leyte. On 20 November 1945 after a series of epileptic convulsions he was admitted to an Army Hospital in Okinawa, where neurological examination revealed choking of the left optic disc, dilated and fixed pupils, and conjugate deviation of the eyes to the left and upward. There was spastic weakness of the right upper extremity, and hyperactive deep tendon reflexes on the right, with absent superficial reflexes on that side. Stools were negative for ova of Schistosoma japonicum. A spinal fluid examination showed 44 lymphocytes. The patient was transferred to the United States, arriving at an Army hospital on 2 January 1946.

Results of Operation

On 17 January 1946 a craniotomy was performed, and a tumor mass removed from deep within the central region of the left parietal lobe of the brain. Histologic examination of the brain revealed findings compatible with Schistosoma japonicum infestation. Shortly afterward his stools were found positive for ova of Schistosoma japonicum, and it was therefore felt that the granulomatous lesion in the brain was due to schistosomiasis.

Medical Therapy

He was given 63 cc. of fuadin intramuscularly in February and March of 1946. On 7 March 1946 his stools were again positive for Schistosoma japonicum, and he was transferred to another Army hospital for more adequate treatment. On 3 April 1946 ova of Schistosoma japonicum were again found in his stools, and he was given a 30-day course of 2.25 grams of intravenous tartar emetic. Subsequently he had 28 stools specifically examined for ova of Schistosoma japonicum, and they were all negative. As he continued to have convulsions dilantin therapy consisting of 100 mg. each day was instituted.

Progress

Physical examination on admission to Walter Reed Army Hospital was negative, except for tingling, numbness and clumsiness in his right hand, and weak and dizzy spells part of the time. Muscular weakness of his right wrist and hand was noted. He also had blurring of the disc margins bilaterally, and a moderate speech defect. There was minute depression in the left frontoparietal region as evidence of his previous surgery at an Army hospital. Deep reflexes were hyperactive bilaterally. No muscular or sensory changes were noted in the lower extremities.

Laboratory findings: Blood count: Red blood cells, 5,000,000 per cubic millimeter; hemoglobin, 15 grams (Turner's method); white blood count, 6,350 per cubic millimeter; neutrophils, 53% lymphocytes, 32%; eosinophils, 13%; basophils, 2%. Urinalysis, negative. Spinal fluid showed normal pressure and normal chemistry. Six stools were negative for ova of Schistosoma japonicum. Hookworm ova were found in the stools. Xray of the chest was negative. An electrocardiogram showed regular sinus rhythm, and elevated RT segments, leads II and III.

During the month that we observed the patient he had one generalized convulsive seizure. He continued taking dilantin each day and was discharged from the hospital with essentially the same neurological findings as he had on admission.

This fifth patient had a very optimistic outlook on life in spite of his many convulsive seizures before and after his operation. Dilantin was very effective in preventing seizures. The residuals of weakness and speech defect were probably not permanent since only 13 months elapsed from the beginning of his present illness to the time of discharge. The high eosinophile count that persisted for a whole year is of considerable interest.

Case 6

Early Symptoms

A 27-year-old patient who arrived on Leyte in November 1944 and on many occasions bathed in fresh water there was hospitalized on 30 January, 1945, because of weakness and insomnia. At that time he was

very uncooperative, poorly oriented, and had urinary incontinence. During the first week of hospitalization he became comatose with signs of multiple nervous system involvement, along with marked spasticity and rigidity of all of his extremities. A diagnosis of schistosomiasis with cerebral involvement was made after several stool examinations revealed the presence of ova of Schistosoma japonicum. He was treated with 45 cc. of fuadin from 2 February to 22 February, with definite improvement. From 26 February to 16 March he received 45 cc. of fuadin, making a total of 90 cc. After this treatment he was evacuated to the Zone of the Interior and arrived at an Army hospital on 26 June 1945.

Physical examination there revealed an enlargement of the liver three cm below the right costal margin, and bilateral positive ankle clonus with coarse hand tremor. He also exhibited memory difficulties and motor aphasia. He was given two courses of treatment for Schistosoma japonicum infestation: the first consisting of 1.8 grams of tartar emetic from 30 June to 30 July 1945, the second of 100 cc. of fuadin from 16 September to 18 September. In April 1946 he received 2.22 grams of tartar emetic given intravenously. On admission to Walter Reed Army Hospital there was nervousness, tremors, poor memory, and difficulty in walking and in using the right word.

Physical examination revealed tenderness in the right upper quadrant, and the liver was one cm below the right costal margin. Neurological examination showed marked weakness in the left upper and lower extremities. Reflexes were hyperactive bilaterally; ankle clonus was present on the left; there was a small area of anesthesia on the dorsum of the left foot and on the left hand, and there was slight blurring of the margin of the optic discs bilaterally. He had a very poor memory and a little speech defect.

Laboratory work: Red blood cells, 5,000,000 cells per cubic millimeter; hemoglobin, 14.3 grams (Turner's method); white blood cells, 10,000 per cubic millimeter; neutrophils, 74%; lymphocytes, 23%; eosinophils, 2%; basophils, 1%; icteric index, 4% cephalin flocculation, negative; corrected sedimentation rate, 2; 20 stool examinations, negative for ova of Schistosoma japonicum.

End Result

The patient complained continuously of muscle weakness, muscle cramps and headaches. His condition improved only slightly on a regimen of active and passive physical therapy. The neuropsychiatrist disclosed a psychotic reaction in which auditory hallucinations, paranoid trends and memory impairment were the most significant features.

This sixth patient was of considerable interest from many standpoints. He was comatose on one occasion but never had any generalized convulsive seizures. His stools were positive for ova of Schistosoma japonicum during his first admission to the hospital. He was diagnosed and treated soon after the onset of his initial symptoms, but he never completely recovered. The psychotic reaction that he manifested was not found in any of the other nine patients and is unusual as far as the cases recorded in the literature are concerned. It is felt that he will not improve any further since it was approximately two years from the onset of his present illness until his discharge. The cells damaged in the brain will probably never recover.

Case 7

Early History and Symptoms

A 25-year-old white male, captured by Japanese at Bataan in April 1942, was on the Death March for 12 days with almost no food while marching 100 miles. He was a prisoner for 3½ years at Mindanao. During that time he had approximately 70 attacks of dysentery, with blood and mucus, nausea, vomiting and tenesmus. He received sulfonamide therapy for his diarrhea. Since his liberation and for the past year and a half, he has had diarrhea, alternating with periods of constipation. As a prisoner of war he developed a tingling and severe burning of the plantar surfaces of both feet, followed by swelling of the ankles, feet, legs, hands and face. This was interpreted as the wet and dry stages of beriberi. The tingling persisted for almost a year and, for a period of time, was accompanied by paralysis bilaterally from the hips down. The burning decreased following vitamin B_1 injections, and the paralysis subsided; however, the numbness and tingling continued in his toes and fingers.

Cerebral Symptoms

In 1943, approximately one year after the patient was captured, he began to have sudden generalized convulsive seizures, not particularly related to any activity, time of day or emotional strain. After regaining conscious he would remain weak for several hours. These attacks occurred two to three times a week for the first six months, and then once every two months. Preceding these attacks he experienced sensations of being off balance, particularly when arising from a sitting or lying position. The room appeared tilted for just a few minutes, and then his vision spontaneously corrected itself. As a prisoner of war he had also experienced bleeding gums, areas of anesthesia of the palate, and cheilosis, all of which have since subsided, except for bleeding of his gums while brushing his teeth. He has persistent fatigue and, from time to time, nausea and vomiting, both of which were quite severe while he was a prisoner of war. His symptoms cleared up for several months immediately after his release, but it then recurred, and is still present, especially after breakfast. When he was captured, he weighed 145 pounds. He weighed 111 pounds on release. His lowest weight was 84 pounds; he now weighs 145 pounds.

Physical examination on admission to Walter Reed Army Hospital was essentially negative, except for tenderness over the abdomen, neuritic pains in both legs, flabby musculature, decreased sensation to pain and light touch at the ends of fingers and toes, and blood pressure of 120/90.

Laboratory findings: Parasites and ova: Trichuris trichiura and *Schistosoma japonicum ova*. Blood count: red blood cells, 5,650,000 per cubic millimeter; hemoglobin, 15.5 grams (Turner's method); white blood cells, 12,000 per cubic millimeter; neutrophils, 54; lymphocytes.

45; eosinophils, 1. Sedimentation rate, 2. Total proteins, 8.9 grams percent; albumin, 6.25 grams percent; globulin, 2.65 grams percent; albumin-globulin ratio, 2.36. Xray of the chest, negative. Barium enema, negative. Proctoscopic examination, negative.

Provocative Treatment

This patient was immediately started on multivitamin therapy, supplemented by vitamin B_1 injections in view of the residuals of beriberi that were evident. Approximately 20 stool examinations were negative for Schistosoma japonicum ova; however Trichocephalus trichiura ova were found on several examinations. Since this patient had a history suggestive of exposure to schistosomiasis and intermittent diffuse abdominal tenderness with cerebral symptoms similar to those experienced by other patients having cerebral schistosomiasis, it was decided that he should receive a course of tartar emetic therapy. This was started on 9 June 1947, up to a total of 2.22 grams. After the fifth injection his stools became positive for ova of Schistosoma japonicum. He experienced little toxicity to the tartar emetic until after 15 days of therapy consisting of 0.9 grams. The toxic symptoms, which consisted of generalized aching and nausea, continued until the completion of therapy. A generalized convulsive seizure occurred 15 days after the onset of this therapy. There was marked improvement following the tartar emetic therapy, and during the subsequent four months there were no convulsive seizures.

This seventh patient was one of the prisoners of war who had constant exposure to the cerceriae of Schistosoma japonicum for approximately three years. He is one of the few who developed cerebral manifestations and also one of the few that showed ova in their stools after the beginning of antimony therapy. It is felt that his prognosis is excellent and that he may have a complete cure.

Case 8

Exposure and Early Symptoms

A 26-year-old white male was exposed to schistosomiasis while bathing in a stream in Leyte in December 1944. He continued in his usual state of good health until the last week of January 1945, at which time he developed diarrhea, blurring of vision, weakness, manual stiffness and clumsiness, but no significant rash or urticaria at that time. There was no abdominal or muscular pain, but occasional nausea and vomiting. He was hospitalized at a general hospital overseas on 1 February 1945 with headache, fever and mental confusion. The medical officers thought that he had a psychosis of a catatonic type. His history stated that during the first two weeks of hospitalization he was irrational. His white count showed a moderate leukocytosis with a marked eosinophilia. His low-grade fever suddenly rose to 107 degrees after the first week. Repeated spinal fluid examinations were not remarkable. One stool examination was performed and was negative for schistosomiasis; however, since schistosomiasis was very prevalent in that area, he was given a course of fuadin consisting of 40 cc. with little improvement.

Cerebral Symptoms

During the latter part of February 1945 he developed signs of a spastic quadriplegia with a positive Babinski on both sides. His eosinophilia persisted and his sedimentation rate became elevated. During early March 1945 he received a second course of fuadin with marked improvement in strength. He was evacuated to another general hospital in May 1945 where it was revealed that he had a spasticity of the legs with atrophy and hyperreflexia and a negative Babinski bilaterally. Marked weakness in the hands and eosinophilia were also noted. Spinal fluid examination remained negative. On 15 June 1945 Schistosoma japonicum ova were found in his stools, and he was then given a 30-day course of tartar emetic intravenously, up to a total of 1.8 grams. Following this course of therapy there was some improvement in his strength; but during the following six months the patient noted little subjective improvement. His appetite was good, but he was still 10 pounds underweight. He noted some right upper quadrant pain during November 1945, and was started on another course of tartar emetic; but as it produced a dermatitis, it was discontinued. He was started on fuadin in March 1946, but this was also discontinued because a dermatitis appeared on the fourth injection.

Disabling End Result

He was transferred to an Army hospital on 9 April 1946. He was somewhat improved, but showed generalized hyperreflexia with absence of the superficial reflexes. There was a flaking of the skin over the entire body with a mild redness. Motor power was good in the upper extremities, but was definitely impaired in the trunk and legs. There was diffuse atrophy. A positive Babinski and Hoffmann were present bilaterally, also ankle and patellar clonus bilaterally of the sustained type. There was a 4% eosinophil count and a sedimentation rate of 4 mm. The electroencephalogram was essentially negative. The patient was fitted with a drop foot brace with ankle straps. A regimen of prostigmine and extensive physiotherapy was instituted, but no great change was noted in the spasticity during and after treatment.

The patient was transferred to Walter Reed Army Hospital on 9 November 1946. During his 10-month stay there he was given extensive physiotherapy treatment. Walking became satisfactory with the aid of canes. His mental attitude improved remarkably, and he was able to pass his examination for a driver's license, using a hand-controlled car. However, the generalized spasticity and weakness in all muscles persisted.

This eighth patient demonstrated the most severe residuals we have seen. He was followed for more than two years, and it is felt that the generalized spasticity and weakness in all muscles are permanent. He represents one of the few cases with bilateral and diffuse involvement; the symptoms and signs were usually localized to the right or left side. He was given two courses of fuadin therapy before ova of Schistosoma japonicum were found in his stools.

Case 9

A 27-year-old patient, a prisoner of the Japanese on Mindanao from 1942 until February 1945, suffered dur-

ng that time from malnutrition, avitaminosis, malaria, hookworm infestation and various undiagnosed types of dysentery. He was liberated in February 1945 and was immediately evacuated to the United States.

Cerebral Symptoms

Because of neurological symptoms suggestive of brain tumor he was transferred to an Army hospital, where he was found to have intestinal schistosomiasis with cerebral manifestations and where he was treated with two courses of fuadin consisting of 45 cc. each. In January 1946 he was transferred to another Army hospital and was in fairly good health except for fatigability, photophobia, a tendency to become mentally fatigued, and loss of strength in the left arm and leg. He also had mild tinnitus with occasional sporadic attacks of diarrhea.

Physical examination was essentially negative except for muscular weakness of the left arm and leg.

Laboratory data revealed red blood cells of 5,270,000 per cubic millimeter; hemoglobin of 15.5 grams (Turner's method); white blood cells of 10,400 per cubic millimeter; neutrophils, 54%; lymphocytes, 37%; monocytes, 4%, and eosinophils, 5%. Stool examination was positive for Schistosoma japonicum ova on 21 January 1946. Bromsulfalein test showed 10% retention in 45 minutes. Icteric index was 4. Schistosomiasis skin test was positive. Eosinophile count varied from 10% to 14%. Blood urea nitrogen was 14 milligrams percent. Bromsulfalein test revealed 25% retention in 45 minutes on one occasion and 6% retention in 45 minutes after 15 days. Following the initial finding of Schistosoma japonicum ova approximately 30 stools were negative for pathogenic parasites and ova. Repeated blood counts showed diminution of the eosinophils to 3%. Thymol turbidity was 5.7 units. A spinal tap was done and showed no white or red blood cells, but did reveal a positive globulin and a spinal fluid protein of 48 milligrams percent. The spinal fluid smear was negative for ova of Schistosoma japonicum. The patient was seen by a psychiatric consultant who felt that he had organic brain disturbance and that his intelligence quotient was very high. The patient was also seen by the tropical disease consultant, who confirmed the diagnosis of chronic schistosomiasis, intestinal and cerebral, and who felt that further therapy for infection with Schistosoma japonicum should be instituted. The patient continued to show marked improvement.

Deterioration

It was believed that the central nervous system defects were demonstrable only on special psychological testing and that repeated bromsulfalein tests should be done and stool examinations evaluated further. Following a course of 100 cc. of fuadin therapy the patient developed a hepatitis with abnormal bromsulfalein retention and a moderately increased icteric index. On a high carbohydrate, high protein, low fat diet with vitamin supplements the nausea and anorexia subsided. In June 1946 he felt that he was declining, having increased fatigability, return of tinnitus, a mild feeling of confusion, particularly when tired, and considerable memory loss. Because of this symptomatology he was given a 30-day course of 2.22 grams of tartar emetic. The tartar emetic was well tolerated, and resulted in considerable subjective improvement, which continued during the following month. Still present, however, were clumsiness of the left hand and a very slight tendency to sway backward upon shutting his eyes.

Physical examination on admission to Walter Reed Army Hospital was essentially negative except for muscle weakness of the left arm and leg; it was also noted that he talked very slowly and was very self-conscious. He was placed on physiotherapy and symptomatic care, but he improved very little during six months of observation.

This ninth patient was a major in the infantry: the only officer I know who developed cerebral manifestations from his schistosomiasis. He was more concerned about his future than the enlisted men since he had a "superior type of mind" prior to his infection. I think that the remaining problem in this patient was continuous psychotherapy. He will probably return to near normal only after years of psychiatric help.

Case 10

Exposure and Symptoms

A 25-year-old black male was stationed at New Guinea from December 1943 to November 1944, and on Leyte from November 1944 to May 1945. His present illness began on 18 January 1945 while he was on Leyte. He had bathed and washed clothes in the local rivers until December 1944; and he was continuously in swampy water and rice paddies while on an engineering construction project. During this time there was no record suggestive of a cercarial rash. The present illness began with rapid swelling about the face, trunk, and upper extremities, with associated mild upper abdominal pain not localized to either the right or the left side. The patient turned in on sick call on 24 January 1945 at an Army hospital. During the subsequent month, he could not recall what had transpired.

Cerebral Symptoms

A perusal of the incomplete records revealed that the patient was semicomatose, running an intermittent pyrexia up to 102.6°, and was incontinent of urine and feces. He was in a deep lethargy and when aroused would complain of upper abdominal and chest pain. During this period neurological examination revealed marked weakness in the left arm and leg, with ankle clonus and hyperactive deep reflexes on the left side. The white blood count did not exceed 8,600, and the highest eosinophilic count was 60%. On 5 March an Xray of the chest disclosed a hazy mottling over the lower half of each thorax. The stools were repeatedly negative for ova of Schistosoma japonicum, but it was decided to treat him for schistosomiasis because of the history and clinical picture.

He was given 1.42 grams of tartar emetic intravenously from 10 February 1945 to 4 March 1945 with gradual improvement in his general condition. Because of depression of the T waves in all leads in the electrocardiogram, it was decided to discontinue the above medication, and fuadin was begun intramuscularly, 25 cc. being given between 6 March 1945 and 12 March 1945. After this therapy he was greatly improved and was returned to the United States on 11 May 1945 with mild residual weakness of the left arm and leg.

On admission to an Army hospital on 8 June 1945, the patient's only complaints were fatigability and the fact that he was 20 pounds under his normal weight. There was an eosinophilic count of 14%. Repeated stools were negative for ova of Schistosoma japonicum, but one examination showed a few Anyclostoma duodenale and Trichocephalus trichuria ova. He was transferred to Walter Reed Army Hospital on 7 October 1945 for further therapy.

Physical examination on admission was essentially negative except for weakness of the left arm and leg. Deep reflexes were hyperactive on the left side, but no ankle clonus was elicited. He was 10 pounds underweight.

Laboratory findings were as follows: Red blood count, 4,600,000 per cubic millimeter; hemoglobin, 14 grams (Turner's method); white blood count, 7,800 cells per cubic millimeter; neutrophils, 57%, lymphocytes, 39%, eosinophils, 4%. Stools to the laboratory for ova of Schistosoma japonicum, 36 megative. Proctoscopic examination revealed a few submucosal hemorrhages in July 1945 and was negative in November 1945.

He was placed on extensive physiotherapy treatments and his left arm and leg both became somewhat stronger. During the subsequent six months, however, there was no further improvement.

This tenth patient was exposed to the cerceriae of Schistosoma japonicum on several occasions. His fever during the acute onset of his disease was probably the highest recorded in the patients with cerebral schistosomiasis. His electrocardiogram showed depression of the T waves, but treatment was continued until the course was finished. He had very few residuals when discharged from the hospital.

Summary

1. A summary of the literature on cerebral schistosomiasis is presented.
2. Ten case histories are given with an average follow-up of 18 months.
3. A discussion of the 10 cases is presented with a view to bringing out some of the important points in diagnosis and treatment of cerebral schistosomiasis.
4. Cerebral schistosomiasis should be considered in the differential diagnosis of patients who have symptoms and signs suggestive of a brain tumor and who have been in an endemic area.
5. Combined medical and surgical treatment is necessary in some patients.
6. Ova of Schistosoma japonicum may not be found in the stools of patients having symptoms and signs of cerebral schistosomiasis.
7. Extensive treatment consisting of several courses of tartar emetic should be given every patient diagnosed as having cerebral schistosomiasis.
8. Cerebral schistosomiasis patients should be followed for a minimum of two years.
9. One can expect no further improvement in the residual manifestations of cerebral schistosomiasis after two years.

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In one night the ravages of half a century had passed over my face. Nor have my nerves ever recovered their tone after that dire shock. Can you wonder that my life was blighted, that my lover shrank from me, so sad a wreck was I?*

*Anonymous, Blackwood's Edinburgh Magazine, January 1861.

Spinal Cord Injury

Some Psychological Considerations

ALAN H. ROBERTS, PH.D.

It is paradoxical that, while the bulk of the literature published on spinal cord injury emphasizes the medical issues, some of the major problems are psychological and social. The psychological aspects of the spinal cord injured patient have not been adequately studied or evaluated.

When an individual sustains a spinal cord injury, the first concerns of both the physician and the patient are obviously medical. The patient's acute injury is treated to insure his survival and to minimize the extent of injury. Laminectomy may be performed and there is a period of immobilization for fusion of vertebrae or stabilization of fractures at the site of injury. Once these problems have been treated, long range medical care becomes supportive and inextricably intermixed with psychological and social adjustment. Examples of problems of medical care with these implications include skin hygiene to prevent ischemic ulcers, prevention of urinary tract infection, dietary supplementation, control of spasticity, control of excretory functions and sexual malfunction. The social and psychological components of all of these problems must be taken into consideration if the patient is to make an optimal adjustment.

Motivational, emotional, interpersonal, and vocational problems inevitably originate following the onset of paraplegia. The psycho-social problems require as much emphasis as the purely medical problems in the total ongoing rehabilitation of the patient. Indeed, as Braceland[1] has pointed out: "Medicine is finding that to fulfill its obligations in a changing epidemiology and a changing culture, it is not enough to apply the insights and techniques of pure science. It is equally important to treat the patient against the background of his environment and in light of the personal, interpersonal, and social meaning of the illness."

The long range adjustment of the patient who sustains a spinal cord injury is determined by two primary factors: (1) the premorbid adjustment of the patient and (2) how the patient works through and accepts his disability.

The best predictor of future behavior is past behavior. The greater the degree of "ego strength" possessed by the patient, the better the adjustment to his disability is likely to be. "Ego strength" is determined by the patient's possession of most or all of the following characteristics:[2] good physical functioning, spontaneity, the ability to share emotional experiences, conventional but not fundamental or dogmatic religious beliefs, permissive morality, good contact with reality, feelings of personal adequacy and vitality, physical courage, and lack of fear. Individuals with high ego strength are generally much better able to cope with severe stress than individuals who lack these characteristics. In spite of isolated examples of individuals who became "better people" from a social standpoint after injury than before, generally, severe stress is more likely to disrupt a personality than to improve it. The less well adjusted a person is prior to injury, the more likely he is to have difficulties following the stress.

The person with greater intellectual ability has more opportunities to engage in a variety of activities following his disability than the person with less intellectual ability. However, it is not simply the degree of intelligence but the kind of intelligence, the intellectual orientation of the patient, that affects his future adjustment. The intelligence of some people tends to be channeled into verbal thinking, others tend to have a bodily orientation and they are more concerned with physical interests.

The person whose bodily functioning is severely disrupted by a spinal cord injury will have a better chance of realigning his life if his interests center

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on verbal-intellectual pursuits rather than on physical. Unfortunately physically oriented individuals are the ones who engage in the type of activities that increase the probability of accidents.

Impulsivity vs. the ability to delay gratification, other facets of premorbid personality, also have an important bearing on post-traumatic adjustmen.[3,4] A reasonable adjustment to a spinal cord injury would logically require that the patient be able to sustain effort, plan ahead, and delay immediate gratification in favor of more important long-range goals. Again, individuals most likely to sustain traumatic injuries to their spinal cords are those who show more than average impulsivity.

The single most important contribution that the physician can make to the future adjustment of the patient is to inform him as early as possible, and as clearly as possible, about the nature of his injury and his prognosis. Most patients in early stages are not clearly informed of the fact that they have an exceedingly low probability of ever walking.

Two rationalizations are usually given by physicians for delay in informing the patient. First, the physician feels that if he exaggerates the extent of the future disability and is wrong (i.e., if the patient happens to be one of the few who recover function), the patient's faith in physicians will be disturbed. Actually, in the two or three instances that we have observed of a patient recovering more function than he was told he would have, the patient has been both grateful and pleased and credited the doctor and the treatment for his improvement. A second reason often given for withholding accurate, but unpleasant, prognostic information is that if the patient is told he will be unable to walk again, "it will destroy his hope" and he will then have no motivation to become rehabilitated. Our own experience is contrary to this. Loss of motivation over a period of time is more often the result of failure by the patient to achieve unrealistic gains which he has been hoping for, usually on the basis of unclear information or information offered *after his unrealistic expectations have been fixed.*

However, withholding accurate and detailed prognostic information deprives the patient of the chance to grieve over his loss and to appropriately work through his feelings about this loss. There is growing recognition[5] that grief is a complex, but stereotyped, response pattern that includes both psychological and physiological symptoms such as withdrawal, fatigue, sleep disturbance, and loss of appetite. Averill[5] believes that grief is fundamentally a biological phenomenon whose function is related to the maintenance of long-term social bonds. The usual occasion for grief is the loss of a significant object: another person such as a close relative; material things such as wealth; or even a symbolic object such as one's reputation. However, grief may stem not only from the loss of an object, but also from a change in social relationships or in social roles.[6,7] If a change in social role is viewed as an important factor in grief reactions, then grief as a response to a loss of body function is readily explained. Bibring[8] and Becker[9] suggest that grief reactions occur primarily when the change in role leads to loss of self-esteem or otherwise causes the person to feel that his behavior lacks meaning or rationale.

The patient who builds up his defenses against an awareness of loss before he is directly told about that loss, is most likely to continue searching unrealistically for the return of bodily function. When, over a period of months or years, his hopes are unfulfilled, he is likely to suffer a chronic form of depression, a reduction in self-care, and general psychological and physiological deterioration.

The physician can aid the patient in adjusting to his loss by not presenting him with "double messages" concerning his future and prognosis. The practice of standing the paraplegic patient in long-leg braces and offering him a trial of walking during the first weeks or months after the trauma is a common form of double message to the patient. On the one hand, he is told that he is unlikely ever to be able to walk functionally and usefully again; at the same time, a great deal of time and effort by a skilled staff are devoted to teaching him to perform a function that he has previously been told he cannot accomplish.

Some patients demand a trial of walking and this opportunity probably should be given to them. However, the patient should be asked to wait an appropriate period of time before this trial is actually attempted. Since the period of mourning in our society traditionally ranges from three to twelve months the patient should be asked to wait a year and then return for his trial. At that time, when he tries and fails (if indeed he still wishes to try), the effects of the disappointment are likely to be minimized, and his defenses will permit him to respond more appropriately to that

disappointment.

Even the patient with a high degree of "ego strength" will show some degree of "ego decompensation" as the result of the sudden dramatic onset of his injury and loss of function.[10] In addition to the normal brief reaction previously described, typical ego defenses are brought into play and exaggerated. The patient may display symptoms based upon withdrawal, denial, or depression.[11] It must then be determined whether the patient's symptoms constitute a relatively "normal" working through of his reactions to the sudden and serious loss or whether his responses are exaggerated and maladaptive. The most evident characteristic of an abnormal reaction is its excessive nature and its protracted course. When an abnormal reaction is suspected, psychiatric and psychological consultation should be obtained for the purpose of intervening. However, barring a disproportionate reaction, the patient should generally be allowed to work through his feelings concerning his disability at his own pace.

A rehabilitation program that emphasizes activity, motivation, and readjustment may push the patient toward reconstituting experiences before he is ready. The individual is then unable to develop appropriate defenses and new methods of coping with his new situation and new role at his own pace. Perception of this requires great sensitivity on the part of the physician and treatment staff.

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Cover Photograph

"Crystal Wonderland"

The cover photograph was taken by Dr. Vernon Lindberg in 1967 during a heavy sleet storm which hit the Twin Cities. He tells the editors that he went out to Cedar Lake to take the photograph, and being improperly dressed for the cold weather, had difficulty in manipulating the lens and making the proper adjustments to the camera.

Photography is a new hobby with Dr. Lindberg and one which he thoroughly enjoys. He is a member of the Minneapolis Color Photo Club which is the oldest color transparency club in the country, having been in existence for 32 years, and, the first camera club in the country devoted exclusively to color photography.

Dr. Lindberg is a clinical Associate Professor in Ophthalmology at the University of Minnesota Medical School and has offices in the Southdale Medical Building in Minneapolis.

Obstruction of the Common Bile Duct

Duodenal Diverticula

HARRY B. NEEL, M.D.

DUODENAL DIVERTICULA are present in from one to six percent of individuals who have x-ray examinations of the upper gastrointestinal tract.[1] Sixty-two to 83% of the diverticula occur in the second portion of the duodenum and nearly all of them are along the concave side, within 2.5 centimeters of the ampulla of Vater.[2]

Although duodenal diverticulum was first described in 1710,[3] the diagnosis was first made in a living individual in 1913 by Case.[4] Farsell and Key[5] performed the first operation for removal of a diverticulum which had been previously diagnosed. Because indications for removal of duodenal diverticula are not common, the number of reported operations is small. Waugh and Johnston[6] reported that of the 30 patients who had operations for duodenal diverticula at the Mayo Clinic prior to 1955, in only eight was the diverticulum the basic reason for operation. Cattell and Mudge[7] stated that only 25 cases of duodenal diverticula were operated on at the Lahey Clinic in a ten year period.

Although the majority of duodenal diverticula are asymptomatic, the complications which occur in about ten percent of patients with diverticula include ulceration, acute inflammation, perforation, hemorrhage, formation of enteroliths and compression of the common bile duct. An unusual complication is biliary and pancreatic duct obstruction accompanied by pain, cholangitis, jaundice, and fever.

The recurrence or persistence of symptoms after cholecystectomy, referred to by some clinicians as the "post-cholecystectomy syndrome," causes the surgeon to consider the possibility of overlooked stones in the common duct, stricture of the duct, or pancreatitis. Another possibility that should be considered is compression of the common duct by a duodenal diverticulum.

The author has cared for two patients, each of whom had had cholecystectomy, who continued to have attacks of severe pain in the upper abdomen. In one patient jaundice had complicated two of the episodes. In each case a duodenal diverticulum was detected on radiographic examination of the upper gastrointestinal tract. Removal of the diverticulum relieved the symptoms and the patients have remained well.

Case 1

A white woman, age 67 years, without a history of previous gallbladder disease, developed acute cholecystitis in June, 1964. As an emergency procedure, the acutely inflamed gallbladder was removed. One stone was impacted in the cystic duct and the common bile duct was normal in size. Convalescence was entirely uneventful.

The patient was well for four weeks and then she began to have pain in the right upper quadrant of the abdomen each day. Because she thought food produced or accentuated the discomfort, the patient was afraid to eat and she lost weight. She did not have fever, chills, nor jaundice. When the attacks of pain became intolerable, the patient reentered the hospital.

Physical examination was entirely negative. Serum bilirubin was 0.24 milligrams percent and the serum anylase was 90 Somogyi units. Intravenous cholangio-



Fig. 1—Duodenal diverticulum demonstrated by Roentgen examination of upper gastrointestinal tract.

Dr. Neel practices in Albert Lea, Minnesota.



Fig. 2—T-tube cholangiogram which shows duodenal diverticulum filled with dye.



Fig. 3—(Case 2) Duodenal diverticulum shown in upper gastrointestinal roentgen study.

grams revealed slight dilatation of the common bile duct but there was no evidence of any obstruction or calculus. Roentgen examination of the upper gastrointestinal tract disclosed a duodenal diverticulum of moderate size which arose from the second portion of the duodenum (Figure 1).

At operation the common bile duct was dilated, and measured one centimeter in diameter. On opening the duct sandy material escaped, and on exploration of the duct scoops were passed easily into the duodenum. When a T-tube cholangiogram was made the dye passed into the duodenum promptly and the large duodenal diverticulum was filled (Figure 2).

After the diverticulum was exposed by reflecting the duodenum medially, the neck was found to be adjacent to the point at which the common duct entered the duodenum. The diverticulum was excised and the defect in the duodenal wall was closed with two rows of sutures. The T-tube cholangiogram was then normal.

The patient had an uneventful convalescense and she had no further discomfort in the upper abdomen.

Case 2

This patient was a white woman, age 74 years, whose gallbladder had been removed in 1963 because of acute cholecystitis. She remained well until February 1968 when there was onset of upper abdominal pain accom-



Fig. 4—(Case 2) T-tube cholangiogram after removal of the duodenal diverticulum. The common duct was dilated by obstruction caused by diverticulum.

panied by jaundice. The patient was icteric and there was mild tenderness in the right upper quadrant of the abdomen. The results of the pertinent laboratory tests were: Serum bilirubin 5.61 milligrams percent, leukocyte count of 9,900 per cubic millimeter, hemoglobin 14.7 grams, and erythrocyte sedimentation rate 24 millimeters per hour. On examination of the upper gastrointestinal tract a diverticulum was noted in the second portion of the duodenum (Figure 3). Prompt recovery followed institution of medical treatment.

In November, 1968, this woman was again hospitalized because of pain and jaundice. The urine contained two plus bile. The serum bilirubin was 4.4 milligrams percent and declined to 2.2 milligrams percent on November 18. The leukocyte count was 7,400 per cubic millimeter; the sedimentation rate was 24 millimeters per hour. Radiographic examination again showed the duodenal diverticulum which had become larger. Operation was deferred until the patient recovered from a respiratoy infection.

The abdomen was entered through the old upper right rectus scar in December, 1968. The common bile duct was greatly dilated and bile gushed out when the duct was incised. Exploration of the duct did not yield a stone and scoops were passed into the duodenum. The duodenum was reflected medially and an incision was made into it just beyond the pylorus. As the diverticulum was mobilized, putty-like material escaped from it into the duodenum. The opening of the diverticulum was within one centimeter of the ampulla of Vater which was identified and protected by a probe which had been passed down the common bile duct.

After the diverticulum was excised the defect in the duodenum was closed with two rows of sutures. The duodenotomy was extended across the pylorus into the stomach and closed transversely as a pyloroplasty. A T-tube was placed in the common duct and the incision in the duct was snugly closed around the tube. The T-tube cholangiogram did not show any abnormalities except dilation of the biliary tree (Figure 4).

The patient has been well and has had no more attacks of pain.

Summary

Duodenal diverticula are seen in one to six percent of x-ray examinations of the upper gastrointestinal tract. Although most diverticula are asymptomatic and are of no clinical significance, ulceration, perforation, hemorrhage, and enterolith formation may occur and produce symptoms. One of the rarest complications is obstruction of the common bile duct. Two patients whose attacks of pain in the upper abdomen were produced by common bile duct obstruction and whose symptoms were relieved by excision of the diverticula have been described.

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Dr. David Pugh

Dr. David Pugh, 63, a Mayo Clinic senior consultant in diagnostic X-ray, retired from the Clinic.

Dr. Pugh, a native of Rushville, Ind., and a graduate from Indiana University Medical School, joined the Mayo staff in 1942 after a four-year Mayo Graduate School residency.

He has maintained a special interest in metabolic diseases of bone, arthritis and tumors of the bone.

An exhibit on primary hyperparathyroidism he co-authored won a gold medal from the American Society of Clinical Pathologists in 1952.

Dr. Erick Reeber Elected President of Headwaters Medical Society

Dr. Erick Reeber of Bagley was elected president of the Headwaters Medical Society at the society's annual meeting recently. Also elected were Dr. Bruce Wilson of Bemidji, vice president, and Dr. Earl Gregoire of Bemidji, secretary-treasurer.

Anaphylactoid Purpura with Spontaneous Intestinal Perforation

WILLIAM C. DeWOLF, M.D.

SPONTANEOUS INTESTINAL perforation associated with anaphylactoid purpura is rare; only eleven cases have been reported in the world's literature.[1-7] Herein is presented the third reported survival of such a catastrophe.

Case Report

A five-year-old boy was well until three weeks prior to admission when he suddenly developed a purpuric rash, pedal and scrotal edema, and a fever of 101°F. The patient's past history was negative except for an episode of pharyngitis ten days prior to admission. He was admitted to another hospital where a diagnosis of anaphylactoid purpura was made. A course of steroid therapy was instituted and the patient sent home asymptomatic. Approximately one week later he noted the onset of nausea and vomiting and was admitted to this hospital. The vital signs were normal. The patient was somewhat dehydrated with a purpuric rash over the buttocks and distal lower extremities. There was mild diffuse abdominal tenderness. However the patient complained of no abdominal pain.

The initial laboratory data included a normal coagulation profile. Other values included: Hemoglobin 9.6 grams %, hematocrit 28%, white count 20,800 mm^3, BUN 24 mg %, ASO 166 Todd Units. Abdominal roentgenograms revealed a gas pattern compatible with a mid small bowel ileus. The patient had a small amount of hematemesis and hematochezia. Prednisone was started along with nasogastric suction and the patient improved. Four days later the temperature rose to 104°F, the abdomen became distended and bowel sounds were absent. It was thought that the patient had an intestinal perforation. A celiotomy was performed and the child was found to have an ileal-ileal intussusception with two perforations along the mesenteric border approximately 5 mm in diameter distal to the intussusception. The diseased segment of the ileum, measuring approximately 35 cm, was excised and an end to end anastomosis was made. Pathology Report: The specimen consisted of a segment of ileum. The serosa and mucosal surfaces were hyperemic. There was an intramural hemorrhage and partial sloughing of the mucosa. Here, the bowel was dusky red and the wall filled with blood. There were two dime size perforations through the bowel, located approximately in the middle of the specimen and surrounded by hyperemic mucosa and serosa. Some of the sections showed a great deal of hemorrhage into the wall of the small bowel with necrosis of the wall.

The patient was closed with a gastrostomy and was placed on antibiotics. His postoperative course was uneventful until the fourth day when the child again demonstrated increased abdominal pain with a temperature elevation to 105°F. Blood cultures taken at that time were positive for Klebsiella. Because of the possibility of a third ileal perforation, the child was taken back to the operating room where a second celiotomy was performed. Abdominal exploration was negative. The patient's postoperative course was slow and complicated with a fascial dehiscence of his wound. The patient was finally discharged asymptomatic.

Discussion

Anaphylactoid purpura is primarily a medical disease among children classically associated with the triad of rash, abdominal pain and joint pain. Its exact etiology is unknown although it is believed to represent a hypersensitivity reaction resulting in vascular damage with increased capillary permeability. Localized areas of hemorrhage and edema are produced. Systemic involvement may include mucous membranes, joints, the gastrointestinal tract and the kidneys.

Visceral involvement occurs in about 50-60% of the patients[8] and represents the most acutely serious problems in the management of this disease. Intestinal lesions include areas of subserosal and submucosal hemorrhage and edema which correlates well with the associated signs and symptoms of bleeding, abdominal pain and tenderness. On occasion the edematous hemorrhagic bowel may act as a leading point to initiate intussusception, an uncommon and serious complication of this disease. Rarely, when such involved areas are associated with numerous microthrombi, a localized area of mucosa may slough resulting in ulceration and possible perforation.

The challenge to the surgeon is quite obvious in the treatment of this disease. Abdominal pain associated with findings compatible of an acute abdomen can provide an irresistible indication for

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abdominal exploration. Oftentimes it is impossible to differentiate an intestinal hematoma alone from one associated with intussusception or perforation. Each may cause obstruction, a mass, and passage of blood per rectum.

Although the incidence of intussusception and/or perforation is not exactly known, it can be estimated to be exceedingly low. When it occurs it can be fatal unless surgery is performed in time. There can be no disagreement with Wolfson's[9] comment regarding the necessity for early operation: "reviewing all the cases one can only say that a sudden worsening of a purpuric patient by severe colicky abdominal pain and vomiting, by absolute constipation (or passage of bright red blood with fecal material), and by the appearance of an abdominal lump which changes little on repeated examinations should provide a strong indication for laparotomy." The presence of unexplained fever, sudden loss of bowel sounds, free air present on roentgenographic examination and an uncontrollable downhill course all add to the list of indications for supporting prompt surgical intervention.

Summary

A case of anaphylactoid purpura with spontaneous intussusception and intestinal perforation is presented. This presents the twelfth reported case of associated spontaneous perforation with anaphylactoid purpura and the third to survive. Anaphylactoid purpura is an allergic vasculitis which may involve the skin, joints, gastrointestinal tract and the kidneys. Abdominal symptoms closely mimic an acute abdomen which may indeed occur in rare instances. In such cases early operation is imperative.

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Doctor Wilkinson rearranged his room, as was his habit a dozen times in the day. He laid out his large *Quain's Dictionary of Medicine* in the forefront of the table, so as to impress the casual patient that he had ever the best authorities at his elbow. Then he cleared all the little instruments out of his pocket case—the scissors, the forceps, the bistouries, the lancets—and he laid them all out beside the stethoscope, to make as good a show as possible. His ledger, day-book, and visiting-book were spread in front of him. There was no entry in any of them yet, but it would not look well to have the covers too glossy and new, so he rubbed them together, and daubed ink over them. Neither would it be well that any patient should observe that his name was the first in the book, so he filled up the first page of each with notes of imaginary visits paid to nameless patients during the last three weeks. Having done all this, he rested his head upon his hands and relapsed into the terrible occupation of waiting.*

*Arthur Conan Doyle's short story "A False Start," 1894.

OLD DOC HESS SAYS: In anger beware lest you expose your Achilles heel. . . . C.O.R.

Nontraumatic Removal of Foreign Bodies

from the Nose and Ears of Infants and Children

RICHARD P. VIRNIG, M.D.

A DIFFICULT AND traumatic ordeal for parent, patient and physician is the removal of a foreign body from the nose or ear canal of an infant or child. Some of the common foreign bodies which have been inserted into their noses and ears by children are: corn, dried field corn or cooked niblets, soy beans, folded bits of paper, small toys and jewelry, especially earrings and sets that have come out of rings.

Admission of the child with a foreign body in the nose and ear to the hospital, administration of a general anesthetic, and removal of the foreign body by irrigation or gentle manipulation is an acceptable method of treatment. This is expensive and inconvenient, and the administration of an anesthetic is not innocuous. The foreign body may be aspirated into the trachea.

A method of extracting foreign bodies from the ear or nose which can be done at once, in the doctor's office, without anesthesia, without risk, and with little discomfort, is my preference. When it has been determined that there is a foreign body in the ear or nose of a child, the child is well restrained with velcro straps or a sheet which immobilizes the arms and legs. A nurse then holds the patient firmly. A Fogarty biliary catheter is tested to determine the amount of air necessary for satisfactory inflation of the balloon and a 2 cc plastic syringe is attached to the catheter. The tip of the catheter is then passed beyond the foreign body, the balloon is inflated and the catheter and foreign body are withdrawn.

For foreign bodies in the nose the catheter is passed along the floor of the nostril and the balloon is inflated, if it is beyond the foreign body. For foreign bodies in the ear the same procedure is followed. If the foreign body is corn or a bean or pea, it has probably swollen, but with care and patience the catheter can be passed and the foreign body removed.

I have used this procedure on numerous occasions and many types of foreign bodies have been successfully removed in this simple manner without anesthesia. In some instances multiple foreign bodies have been found, so it is advisable to examine the nose or ear after recovering the first body. A three-year-old girl was brought to the Clinic because of foul breath. Examination of the mouth and throat revealed no abnormalities. There was considerable discharge from the right nostril and a piece of folded paper, which measured 2x3 inches when unfolded, was removed. Further examination with the speculum showed another piece of folded paper.

A recent case was an eighteen-month-old boy who had been served niblet corn for supper. The mother saw the child push a niblet of corn into the right nostril and attempts to retrieve it were unsuccessful. In the hospital emergency room the niblet of cooked corn was easily removed with the biliary balloon catheter. Another niblet was found higher in the nostril and this, too, was removed with the catheter.

Summary

Foreign bodies in the nose and ears of children can be removed by passing the Fogarty biliary catheter beyond the foreign body, inflating the balloon and withdrawing the inflated balloon and foreign body. Hospitalization and anesthesia are not necessary. Multiple foreign bodies are sometimes present and should not be overlooked.

Wells, Minnesota.

Friendship: State of being attached to another by esteem, respect, and affection.

Historic Hospitals

The New York Hospital, 1771-1971



The New York Hospital, its first building facing east toward Broadway, as it appeared about 1811. Courtesy National Library of Medicine, Bethesda, Maryland.

Last year the New York Hospital observed the two hundredth anniversary of its foundation. Its royal charter, granted by King George III, established "The Society of the Hospital in the City of New York in America" on June 13, 1771.

The hospital has encountered adversity in its building projects. The first building burned to its stone foundation before completion. The rebuilding was interrupted by the Revolutionary War, the uncompleted structure being used as barracks for Continental troops and later for Hessian soldiers after the city was occupied by the British. The famous "Doctors Mob Riot," sparked by public indignation at dissection of cadavers (and by grave robbing), began at the hospital in 1788 where the teaching of anatomy was already under way. Not until 1791, twenty years after the beginning, was the hospital ready to receive patients.

The third and present building, which houses the New York Hospital-Cornell Medical Center along York Avenue from Sixty-eighth to Seventy-first Streets, was under construction at the time of the stock market crash in 1929. The hospital's investments had to be liquidated at low prices, the number of beds reduced, and equipment temporarily omitted on several floors.

In spite of these and other hardships the New York Hospital has contributed importantly to patient care, medical teaching, and medical research. The hospital pharmacopoeia built up by its early apothocaries served as a basis for, and ultimately became a part of the U. S. Pharmacopoeia of today. During the Civil War the hospital treated nearly three thousand soldiers under contract with the Federal Government. In 1927 it entered into an agreement of organic association with Cornell University, becoming a primary teaching hospital.

Although a charity hospital in the beginning, it early accepted private patients, first providing private rooms about 1858. Gradually the proportion of private patients has increased to the present day when health insurance and government programs are beginning to obscure the distinction.

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Minneapolis, Minnesota

Larrabee, Eric: The Benevolent and Necessary Institution, Doubleday & Co., 1971.



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UNCOMMON RELIEF FOR COLD SYMPTOMS

If you've seen one, have you really seen them all?

The following patient profiles represent typical clinical situations, but do not necessarily represent actual cases.

Age 22, previously normal me
with occasional menorrhagia.
on a sequential O.C. for four r
Complains of heavy flow,
occasional intracyclic bleedin
edema, tender swollen breast
Indicates estrogen excess.
1st choice: Switch to a com
bination 50-mcg.-estrogen O.C
(such as **Demulen***).

Age 19, small breasts, minor hirsutism, oily hair and skin. History of metrorrhagia, skipped or scanty menses. New user.
Indicates androgenic excess or estrogen deficiency (fertility is suspect).
1st choice: An estrogen-dominant O.C. (such as **Enovid-E***).

Age 25, average frame, poor complexion. No problem with menses, normal para 1. On a low-estrogen/high-progestogen O.C. for two years. Now complains of scanty flow, decreased libido, depression.
Indicates probable buildup of progestogen-related side effects.
1st choice: Switch to a center-spectrum O.C. with more estrogen, less progestational activity (such as **Ovulen***).

Age 21, short, mammose, with normal menses, some acne. Was put on prenuptial regimen of 50-mcg.-estrogen/moderate-progestogen O.C. for two months. Now has increased acne.
Indicates metabolic production of androgen or relative estrogen deficiency.
1st choice: Switch to a 100-mcg.-estrogen combination (such as **Enovid-E*** or a sequential).



Unmasked, physiologically and anatomically, they're not all the same. A basic difference lies in their hormone profiles. One may secrete too much estrogen, another not enough...or perhaps too much androgen; the vast majority would fit somewhere into the broad center spectrum.

Although the profiles described below may not be completely predictive, in optimal O.C. selection, the estrogen-progestogen activity ratio should be carefully matched to the patient profile. Searle offers you O.C.s in a range not only suitable for your patients in the balanced center spectrum, but also adaptable to the patient with another type of hormone profile.

Oral contraceptives are complex medications. Among the commonly reported adverse reactions are: intracycle bleeding, fluid retention, tender or swollen breasts, exacerbation of acne condition, changes in libido, amenorrhea while on medication and upon discontinuance, nausea, leg cramps, headaches, weight gain. Therefore, after reference to the prescribing information, oral contraceptives should be prescribed with care.

*Note: In some patients any level of exogenous estrogen or progestogen may produce symptoms of excess hormone activity.

A 25, tall, slender, athletic, w flat chest. On a progestogen- minant 50-mcg.-estrogen O.C. H recurrent trichomoniasis a Monilia.
ndicates estrogen deficiency and e ess of progestogen in current O.C.
st choice: Switch to a com- b tion pill with 100 mcg. e ogen and less progestational a vity (such as **Enovid-E*** or len or a sequential).

Age 23, "Miss America" figure, previously normal menses, healthy skin and hair. On a 50-mcg.-estrogen pill for four months. Complains of intracyclic bleeding.
Indicates probable need for more estrogen.
1st choice: Switch to a center-spectrum O.C. with more estrogen and moderate progestogen dominance (such as **Ovulen***).

Age 21, college senior, average build. On highly progestogen-dominant/low-dose-estrogen O.C. for six months. Now complains of amenorrhea, between-cycle headaches, weight gain.
Indicates probable progestogen excess.
1st choice: Switch to a center-spectrum pill (such as **Ovulen***).

Age 27, slightly overweight, multiparous. Nausea with all three pregnancies and with a sequential O.C. three years ago. Has pre-menstrual fluid retention and leg cramps.
Indicates probable excess of estrogen.
1st choice: A 50-mcg.-estrogen/progestogen-dominant pill (such as **Demulen***).



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prescribing information,
ease see next page.

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Actions – Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note – Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication – Ovulen and Demulen are indicated for oral contraception.

Contraindications – Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings – The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions – The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any poss influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adre hepatic or uterine function awaits further study. A decrease in glucose tolera has been observed in a significant percentage of patients on oral contra tives. The mechanism of this decrease is obscure. For this reason, diabetic tients should be carefully observed while receiving Ovulen or Demulen ther The age of the patient constitutes no absolute limiting factor, although treatm with Ovulen or Demulen may mask the onset of the climacteric. The patholo should be advised of Ovulen or Demulen therapy when relevant specimens submitted. Susceptible women may experience an increase in blood pres following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives – A statistically significant association has been demonstrated betw use of oral contraceptives and the following serious adverse reactions: throm phlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relat ship has been neither confirmed nor refuted for the following serious adve reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdo inal cramps and bloating), breakthrough bleeding, spotting, change in menstr flow, amenorrhea during and after treatment, edema, chloasma or melas breast changes (tenderness, enlargement and secretion), change in we (increase or decrease), changes in cervical erosion and cervical secretions, s pression of lactation when given immediately post partum, cholestatic jaund migraine, rash (allergic), rise in blood pressure in susceptible individuals a mental depression.

Although the following adverse reactions have been reported in users oral contraceptives, an association has been neither confirmed nor refut anovulation post treatment, premenstrual-like syndrome, changes in libi changes in appetite, cystitis-like syndrome, headache, nervousness, di ness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforr erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral cont ceptives: hepatic function: increased sulfobromophthalein retention and otl tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and thyroid function: increase in PBI and butanol extractable protein bound iodi and decrease in T^3 uptake values, metyrapone test and pregnanediol det mination.

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Indication – Enovid-E is indicated for oral contraception.

The *Special Note*, *Contraindications*, *Warnings*, *Precautions* and *Adver Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E a should be observed when prescribing Enovid-E.

Enovid-E®

brand of norethynodrel with mestranol

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Where "The Pill" Began



Editorials

Regionalization in Minnesota

With this issue subscribers to Minnesota Medicine receive a supplement containing ten reports on activities supported by Northlands Regional Medical Program, Inc. (NRMP). It has been a rewarding experience to serve as "Guest Editor" for this supplement and write the lead article. In line with early NRMP program emphasis, the articles deal with multiple facets of continuing education for health-related personnel and education of patients and their families. Included are physicians, nurses, nutritionists, laboratory technicians, social workers, hospital administrators, clergymen, patients and the families of patients. The authors write about key health care issues, problems and barriers. These matters not only provide interesting reading but demonstrate the scope of continuing education problems and document various innovative methods.

Special editorials included in this issue provide a form of recognition for the two medical leaders who conceived Northlands Regional Medical Program back in 1965—Dr. Robert B. Howard and Dr. J. Minott Stickney. As Dean of the College of Medical Sciences and President of the Minnesota State Medical Association respectively, Drs. Howard and Stickney laid the foundation for a democratic organization to develop this new federal-private partnership program. The principles these "founding fathers" built into NRMP enabled this initially controversial program to withstand the series of crises of any new movement and emerge stronger for the experience. In this program, as in many others, these esteemed Minnesota physicians inspired many others to high standards of achievements. It is a pleasure to have the opportunity to give them a token of recognition which they so justly deserve.

NRMP is a part of a growing movement in applied research and development. Those of us who witnessed the transition of fundamental research from a labor of love to a public movement have sincere hopes that the current applied research movement can become equally productive. The great challenge of technological discovery is being followed by the equally great challenge of scientific application of new discoveries for the betterment of the whole society.

Future articles in this and other journals will report on currently active projects in areas of Health Manpower and Health Services Development, as well as Education. The regionalization movement seems to have caught on, and participants throughout the state are utilizing rational scientific methods in seeking solutions to our complex health care problems. The persistent "Ferment in Medicine" described so lucidly by Dr. Richard Magraw in 1966 is evolving into a progressive force for constructive change in the health care system in Minnesota.

Winston R. Miller, M.D.
Guest Editor

Dr. Miller is the Program Director, Northlands Regional Medical Program, Inc., St. Paul.

DOCTORS.

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1. Piecemealitis.

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3. Apartmenthousitoma.

An affliction which commonly strikes those in the medical profession who are attracted to get-rich-quick real estate ventures; can cause great financial pain and mental anguish, especially in a market that's overbuilt.

4. Multiple brokerosis.

A state of investment confusion which results from dealing with too many different counselors; characterized by the left hand not knowing what the right hand is doing.

5. Simple neglect.

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NRMP Supplement

THE SUPPLEMENT to this December, 1972 issue of MINNESOTA MEDICINE is a comprehensive report of the activities of the Northlands Regional Medical Program (NRMP). The supplement is dedicated to Mary Jane Ryan, Ph.D., librarian for NRMP, who died this year. Her posthumous article is a lively discussion of hospital and other medical libraries in the State. She describes how physicians, both rural and metropolitan, can use MEDLARS and the new MEDLINES to search medical literature.

Winston Miller, the first director of NRMP, discusses its accomplishments in the five years Northlands has been in existence.

Russell Lucas records a dialogue with his good friend, Sir William Osler.

William R. Fifer points out how a medical audit can be conducted in a community hospital; how it can lead to better medical care by exposing deficiencies to the medical staff willing to let itself be audited.

NRMP came into being during the early development of intensive coronary care units (ICCU) and supported their development and training of personnel to man them. O'Donovan, Mankin et al. describe the mortality of acute myocardial infarctions in the ICCU's as subsiding from 30 to 35% to 22%, a decrease largely due to better care in the earliest hours after the attack. This is a major therapeutic advance.

The RMP concept and its local deployment as the local NRMP as described in the supplement undoubtedly will be enthusiastically commended by many and probably just as enthusiastically condemned by some. All physicians, however, should become acquainted with the activities of this organization.

Reuben Berman, M.D.
Editor

*Supplements are supported by special funds and are printed at no expense to MINNESOTA MEDICINE or the Minnesota State Medical Association.

Historical Development of NRMP

REGIONAL MEDICAL PROGRAMS had their origin under Public Law 89-239. The 89th Congress in 1965 will long be remembered for the legislation affecting the medical profession. It established Medicare and Comprehensive Health Planning in addition to Regional Medical Programs. RMP provided for cooperative relationships between the practicing medical profession and the centers of medical education. The general objective was to bring the latest and best in medical knowledge to the health care delivery system and education was to be an essential ingredient. Because of the impetus from Dean Robert Howard of the University of Minnesota Medical School, an appropriate planning group was gathered together. With great foresight he insisted that the management of the Regional Medical Program should reside outside the two medical schools then in existence; namely, the University of Minnesota College of Medical Science and the Mayo Graduate School of Medicine. In view of the subsequent shift in emphasis from education to health care delivery, the new corporate structure formed by representatives of major medical institutions proved to be very appropriate. Special thanks are due to the University of Minnesota which made funds available before grant monies were obtained, to the Minnesota State Medical Association for making its charitable foundation the original grantee, and to the Mayo Foundation for directing the fiscal affairs for the medical society's foundation in an interim period before a new corporation could be formed. Nine sponsoring institutions provided necessary financial guarantees for the new organization named Northlands Regional Medical Program, Inc.

Those of us who participated in the birth of Northlands Regional Medical Program have often been asked about the selection of the name. The original legislation and subsequent regulations suggested that natural areas of education and practice should prevail and that state lines were not to be rigid boundaries. The name "Northlands" was selected to denote a broad area of



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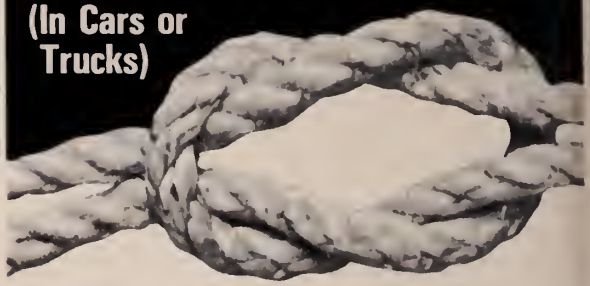
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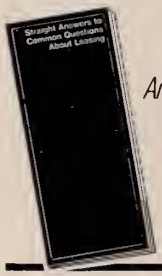
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coverage. Later experience showed that each state wished to have its own Regional Medical Program, and Northlands has been primarily a Minnesota activity. However, our neighbors have been flexible enough to cooperate in some truly regional thinking.

In October, 1967, Dr. Winston R. Miller was appointed to the position of director. He brought an unusual combination of insight and skill to the program. With a background of teaching at the University of Kansas, private practice in Red Wing, Minnesota, and as medical director of the St. Paul Medical Center, Inc. and Director of Medical Education at Miller Hospital in St. Paul, he has been cognizant of the problems in the complex relationships of practicing physicians to the education and health care delivery systems. It is not surprising that he has been recognized by the National Regional Medical Programs as an outstanding leader. Ably assisted by Mr. Robert Wilkins who came from the field of hospital administration, Dr. Miller has assembled an excellent staff. The articles which appear in this Supplement to MINNESOTA MEDICINE demonstrate some of the results of their work.

Regional Medical Programs like other government enterprises recognize the expanding role of the consumer. Those of us who have had the privilege of working with the Regional Advisory Group in which consumers play an important part have had a new and gratifying experience. We are especially grateful to Judge Stephen L. Maxwell of the District Court in St. Paul for his leadership of the Advisory Group during the formative period.

Dr. Miller and Mr. Wilkins with the rest of the staff have fostered the concept that the Regional Medical Program offers an opportunity for the private sector supported by public funds to pursue the goal of bringing improved health care to the citizens of Minnesota. Many in the medical profession (as well as others) originally adopted a watchdog attitude which has now given way to a sense of partnership in innovative studies and activities. With the decision by the Nixon administration to support Regional Programs as a significant part of its approach to the solution of health care problems, all segments in Minnesota, public and private, should be prepared to participate in order to insure the viability of Northlands Regional Medical Program. Sound cooperative efforts by the diverse elements in our health care delivery system are necessary and desirable. Inevitably, there will be more regionalized activity because of the distribution pattern of physicians, the cost of hospital facilities and modern communication methods. Efforts toward such regionalization come in many ways from a variety of sources. Northlands Regional Medical Program has made a significant contribution to the process. It has been both an originator and a catalytic agent.

J. M. Stickney, M.D.
Rochester, Minnesota

Northlands Regional Medical Program, Inc.

I AM GRATEFUL for the opportunity to comment and to participate in this special issue of MINNESOTA MEDICINE, which comprises a timely report on the activities of the Northlands Regional Medical Program (NRMP). In its seven-year history NRMP has made great strides and has many major accomplishments to its credit. The articles in the accompanying supplement, while reporting only a fraction of the activities of NRMP, give ample testimony to the imaginativeness and vigor with which its goals have been pursued by an able staff and by a host of health workers in various cooperating agencies.

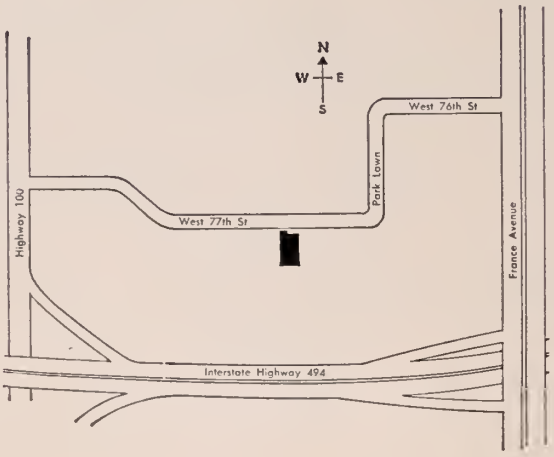
Seven years is surely but a brief segment in the span on our nation's history. It is difficult to realize that so many changes have taken place in so many areas of American life, including health care, during this short period. In the mid-1960s, the public was just beginning to come to an understanding of the seriousness of the shortage and maldistribution of physicians and other health care workers. Further, there was a growing realization that biomedical research alone had not resolved the health care problems of the nation. Despite the notable advances that had been made in understanding biologic phenomena, the fruits of post-World War II research had not effectively been passed on to the average citizen.

Against this backdrop came the report from President Johnson's National Commission—often

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known, for its chairman, as the DeBakey Commission—recommending "A National Program to Conquer Heart Disease, Cancer and Stroke," containing recommendations for the establishment of a series of centers across the nation which would study and treat these disorders. Almost immediately there was substantial concern and attendant opposition from many sources. The medical academic community envisioned the proposed Regional Medical Program (RMP) as a threat to the support of fundamental research. Many practicing physicians saw in it an attempt to replace the existing patterns of medical practice with new agencies that would be government-dominated or government-operated. All physicians and a good many knowledgeable lay people were concerned about a program focusing on heart disease, cancer, and stroke to the apparent exclusion of concern for other kinds of disease that can be equally devastating in their impact.

The final legislation establishing the regional medical program, as passed by both Houses of Congress and signed into law by the President, significantly softened the report of the Commission with respect to the development of treatment centers that might affect patterns of medical practice. The thrust of the legislation was to emphasize the educational and coordinating roles of RMP. The law specifically provided that RMPs should include as key constituents any academic health centers located within their respective jurisdictions.

The leaders of the University of Minnesota College of Medical Sciences and those of the Mayo Institutions joined in sponsoring an organizational meeting to which the officers or other leaders of the other major health care agencies and associations within the state were invited. Early meetings dealt in large measure with organizational concerns and with defining the potential role or roles of the RMP. Not surprisingly, the participating agencies from time to time evidenced concern that the new agency might interfere with or adversely affect their respective functionings. Even in early meetings, however, it was evident that the RMP had become a mechanism whereby, for the first time, agencies with substantial responsibility for the health care of the people in our area were communicating with one another and were discussing at least the possibility of joint action to meet problems of common concern.

The original organizing group was broadened to become even more representative. As mutual confidence grew among members of the group, less time was spent in parochial concern and more time in effective planning for the sound development of an RMP. A program director was subsequently appointed, and this proved to be a happy choice indeed. The Northlands Regional Medical Program has had sound direction by its board and very able administration by Dr. Miller and his staff. As the accompanying supplement records the fact that NRMP has been deeply involved in projects relating to both professional and lay education, others related to the development of health manpower, and still others related quite directly to the provision of health services. Further, NRMP has joined in the sponsorship of both planning and operational projects carried out by other health agencies. At the present time, it is safe to say, any major health care development in the State of Minnesota would necessarily have the active participation of NRMP.

NRMP can look back on a productive and exciting seven years. More importantly, it can look forward to opportunities for even greater accomplishment during the coming years. I am proud to have been among those responsible for giving original impetus to the development of NRMP and for the selection of its director.

Robert B. Howard, M.D.
Minneapolis, Minnesota

I believe when you are in any contest you should work like there is—to the very last minute—a chance to lose it. This is battle, this is politics, this is anything.—Dwight D. Eisenhower

---

Jest breaks no bones.—Samuel Johnson, quoted in Boswell's Life of Johnson.

Respiratory Distress Syndrome

WHEN NEONATAL MORTALITY rates of the United States are compared to many other countries, it would appear that our citizens are receiving second class care. Dr. Martha Burke-Strickland* has pointed the way to improve on these figures. The principal caues of death in the newborn period is respiratory distress syndrome. The infant at risk can be identified and a good result achieved by immediate and adequate treatment. There are however, several road blocks.

One of the frustrations of the busy pediatrician is lack of communication with the equally busy obstetrician. However if these babies at high risk are to be saved, there must be more coordination of effort to reduce this risk. If the amniotic fluid predicts a RDS potential, the pediatrician should be notified so that he can be available to initiate the preventive care as outlined by Dr. Burke-Strickland.

It has been stated that the high neonatal mortality rate in the United States is a social rather than a medical problem. Because of high medical costs and a shortage of medical personnel, optimal care is not achieved.

Many medical insurance policies do not adequately cover the care of the newborn. The high cost of the optimal care may bankrupt the young couple starting out life with meager financial resources.

Recently Dr. Jay Arena, President of the American Academy of Pediatrics, testifying before a U.S. Senate Appropriations Sub-committee, stated "The $900,000 the Department of Health, Education and Welfare will spend for Newborn Intensive Care Units in the fiscal year 1973 is not even enough money to build one mile of interstate highway." These units are costly to build, equip and run. Arena recommended an increased appropriation of $5,000,000. The newborn intensive care unit may not only save a life, but a lifetime.

C. Sherman Hoyt, M.D.
Minneapolis, Minnesota

*Burke-Strickland, Martha: Preventive aspects of respiratory distress syndrome. Minnesota Med 55:9:792, 1972.

Children's Reactions to Hospitalization

WHILE CHILDREN MAY vary in the condition that brings about hospitalization, they all share in the emotional reaction to the experience. All too frequently this reaction is moved to a place of secondary importance in our management of the medical condition. The child's reaction is generally of importance only if there is bothersome behavior to deal with. The quiet or compliant child who is not a management problem does have some feelings about his hospitalization. The noisy or crying child merits consideration over and above our frustration level. Parents in attendance might be more than a bother, though they interfere with the orderly discharge of nursing routines.

Duffy* outlines the scope of the problem and calls it to our attention. I would hope that future articles bring the day-by-day solutions of this problem. We can start now by becoming more aware of the feelings of our young charges. To do this, we have to listen to him.

In a large, modern orthopedic hospital in the East, I was called to see a young boy of 10 who was apathetic and unresponsive to the staff. He had been called into the hospital some days in advance of his surgical procedure, but encountered a delay due to scheduling difficulties. He was observed by the nursing staff to be more and more unresponsive to life around him. A conversation with him rapidly established his perception that he had been left off by his family, was told that he would be *put to sleep* and that his knee would be "fixed." He apparently stopped listening at the "put to sleep" portion of the explanation. (He had a sister who had recently died of a heart condition in her sleep.) On the ward, he saw his roommates one by one placed on carts and whisked off. They did not return. He did not know that the hospital routine was to house postsurgical patients in a recovery area. Therapy for this young man consisted of loading him in a wheelchair to visit the recovery ward where he could establish for himself the reality that his recent friends were alive and in different stages of being well. In like fashion, I found that the patients were acutely aware of the prognosis and progress of fatal illnesses, though they observed *our* rule that they were topics "not to be discussed." Duffy reminds us to engage in the primary prevention of possible emotional difficulties. This is something we can start now.

Ronald Kyllonen, M.D.
Minneapolis, Minnesota

1See page 1168.

Iron therapy for anemia is almost as old as history itself



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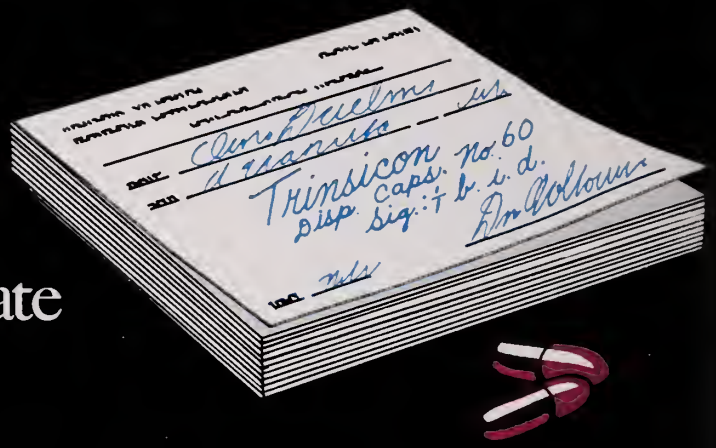
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Potency of intrinsic factor concentrates is determined physiologically, i.e., by their use in patients with pernicious anemia. The liver-stomach concentrate with intrinsic factor and the vitamin B_{12} contained in two Pulvules Trinsicon provide 1½ times the minimum amount of therapeutic agent which, when given daily in an uncomplicated case of pernicious anemia, will produce a satisfactory reticulocyte response and relief of anemia and symptoms.

Concentrates of intrinsic factor derived from hog gastric, pyloric, and duodenal mucosa have been used successfully in patients who lack intrinsic factor. For example, Fouts *et al.* maintained patients with pernicious anemia in clinical remission with oral therapy (liver extracts or intrinsic factor concentrate with vitamin B_{12}) for as long as twenty-nine years.

After total gastrectomy, Ficarra found multifactor preparations taken orally to be "just as effective in maintaining blood levels as any medication that has to be administered parenterally." His study was based on twenty-four patients who had survived for five years after total gastrectomy for cancer and who had been taking two Pulvules Trinsicon daily.

Folic Acid—Folic acid deficiency is the immediate cause of most, if not all, cases of nutritional megaloblastic anemia and of the megaloblastic anemias of pregnancy and infancy; usually, it is also at least partially responsible for the megaloblastic anemias of malabsorption syndromes, e.g., tropical and nontropical sprue.

It is apparent that in vitamin B_{12} deficiency (e.g., pernicious anemia), lack of this vitamin results in impaired utilization of folic acid. There are other evidences of the close folic acid-vitamin B_{12} interrelationship: (1) B_{12} influences the storage, absorption, and utilization of folic acid, and (2), as a deficiency of B_{12} progresses, the requirement for folic acid increases. However, folic acid does not change the requirement for vitamin B_{12}.

Iron—A very common anemia is that due to iron deficiency. In most cases, the response to iron salts is prompt, safe, and predictable. Within limits, the response is quicker and more certain to large doses of iron than to small doses.

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Ascorbic Acid—Vitamin C plays a role in anemia therapy. It augments the conversion of folic acid to its active form, folinic acid. In addition, ascorbic acid promotes the reduction of ferric iron in food to the more readily absorbed ferrous form. Severe and prolonged vitamin C deficiency is associated with an anemia which is usually hypochromic but occasionally megaloblastic in type.

Contraindications and Precautions: Anemia is a manifestation that requires appropriate investigation to determine its cause or causes.

Folic acid *alone* is unwarranted in the treatment of pure vitamin-B_{12}-deficiency states, such as pernicious anemia. Indeed, the use of folic acid in large doses in pernicious anemia without adequate vitamin B_{12} may result in hematologic remission but neurological progression.

As with all preparations containing intrinsic factor, resistance may develop in some cases of pernicious anemia to the potentiation of absorption of physiological doses of vitamin B_{12}. If resistance occurs, parenteral therapy, or oral therapy with so-called massive doses of vitamin B_{12}, may be necessary for adequate treatment of the patient. No single regimen fits all cases, and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential and are recommended.

In extremely rare instances, skin rash suggesting allergy has been noted following the oral administration of liver-stomach material. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Hemochromatosis and hemosiderosis are contraindications to iron therapy.

Adverse Reactions: In rare instances, iron in therapeutic doses produces gastrointestinal reactions, such as diarrhea or constipation. Reducing the dose and administering it with meals will minimize these effects in the iron-sensitive patient.

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Case Report

Intussusception of the Base of the Appendix

ERLING A. KLOPPEDAL, M.D. AND LUIS H. TOLEDO-PEREYRA, M.D.

APPENDICEAL INTUSSUSCEPTION is a rare condition. Only a few cases have been reported in the radiologic[1,3] and surgical literature.[2] Even fewer were those in which the correct diagnosis was made preoperatively.

Two types of appendiceal intussusception may be diagnosed radiologically by means of the barium enema examination[4,5]: (1) complete intussusception of the appendix presenting as a thumb-like mass projecting into the cecum,[6] and (2) partial intussusception of the base of the appendix with or without filling of the appendix by barium. Visualization of the appendix in the latter type is unusual[3] and the case reported below is believed to be only the second published instance of such an occurrence. A third type, in which the appendix intussuscepts into itself, has not been demonstrated radiographically.

The importance of distinguishing a benign cecal lesion from a malignant one is obvious. Included in the differential diagnosis are mucosal, intramural, and extrinsic lesions involving the cecum itself, the appendix, or the ileocecal valve. In most cases direct visualization at surgery will be necessary for diagnosis.

The main predisposing factors in the pathogenesis of intussusception of the base of the appendix are mucocele[7] and foreign body or other conditions that lead to excessive peristalsis of the appendix.

Case Report

A fifty-one year old white male, was admitted to the Veterans Hospital, Minneapolis, with the complaints of abdominal pain, weight loss, food intolerance, and postprandial vomiting. A Billroth II gastrectomy had been performed ten years earlier for duodenal ulcer. Laboratory studies including hemoglobin were within normal limits. An oral cholecystogram showed a single gallstone. Barium enema disclosed a polypoid filling defect in the cecum. A repeat study (Figure 1 and 2) demonstrated association of the defect with the base of the opacified appendix.

At surgery there was an obvious intussusception of the base of the appendix which was easily reduced by manipulation. No other abnormality was found. A simple appendectomy was performed, followed by removal of an elliptical section of the cecum surrounding the base of the appendix. A cholecystectomy was also done. The pathology report indicated cholecystitis with cholelithiasis and a normal appendix and cecum. Recovery from surgery was complete, and the patient's symptoms were relieved.

Dr. Kloppedal is staff radiologist, V.A. Hospital and University of Minnesota, Minneapolis, Minnesota.
Dr. Toledo-Pereyra is resident in surgery, V.A. Hospital and University of Minnesota, Minneapolis, Minnesota.



Fig. 1—Polypoid filling defect in proximal cecum.



Fig. 2—Same defect with the barium-filled appendix. Note the very smooth, symmetrical appearance of the projecting mass, oriented very evenly around the barium-filled appendiceal lumen, fairly certainly ruling out any associated pathology.

Comment

With regard to the surgical treatment of appendiceal intussusception, anything more than simple appendectomy is probably unnecessary. However, some surgeons do recommend anchoring the proximal end of the cecum or the stump of the appendix to surrounding tissues with sutures to prevent future intussusception of the stump and even of the cecum into the ascending colon.

Recently, we learned of two patients with complete invagination of the appendix who were subjected to hemicolectomy because of presumably malignant lesion in the cecum and because of the "no-touch" procedure.[6] It is probable that cecotomy with direct visualization would have led to simple local removal.

In our case the exact preoperative diagnosi was not made initially and hemicolectomy wa considered. A review of the literature, however raised the possibility of a benign intussusceptio of the appendiceal base and resulted in a mor conservative surgical approach.

Summary

Although a rare condition, intussusception o the base of the appendix should be considered i the differential diagnosis of filling defects of th cecum to avoid unnecessary radical surgery. A case is reported in which the anatomy of th lesion was radiographically demonstrated.

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A sound discretion is not so much indicated by never making a mistake as by never repeating it.—Bovee

Healthcaremanship

RICHARD L. REECE, M.D.

"Ordinary health, remember, is highly gambit-prone."—Stephen Potter, One-Upsmanship

SHALL BEGIN by distinguishing between Health are and Healthcaremanship.

Health Care is the serious matter of maintaining ealth, preventing disease, treating illness, and eeding convalescence.

Healthcaremanship, on the other hand, is a ord game. Players match words to outwit each ther. The one who writes or talks the most while ying the least wins.

Healthcaremanship requires experience, knowldge, and forensic skill. Furthermore, healthcareanship is important. It will remain so as long as ere are hearings to be heard, grants to be granted, races to be run, funds to be found, speeches be spoken, words to be written, and listeners r readers to boggle or befuddle. Healthcaremanhip is not essential for these activities, but it helps.

General Gambits

Before I get to specifics, a few words about eneral gambits. In an earlier article,* I deined these as they applied to medical writing. Because these gambits work equally well in Healthcaremanship, I shall review them now.

Gambits	Brief Definition
Windfoggery Weave	Weaving together wind and fog on paper
Retrospective Ramble	Exhaustively reviewing your subject by referring to everything previously written on subject
Humble Hedge	Qualifying your meaning into nothingness by appearing to be humbly objective
Passive Ploy	Writing in passive voice in order to place yourself in background and to divest yourself of responsibility
Word Wedge	Wedging impressive words into sentences where they don't belong
"That" Thrust	Thrusting "That" into start of sentences to avoid direct statements or to conceal them
Verb Void	Voiding sentences of verbs by changing them into nouns in order to lengthen sentences without changing their meaning
Double Dawdle	Doubling word volume but keeping facts constant by using two words of same meaning where one would do
Paragraph Parry	Writing long paragraphs by opening with crisp sentence, then taking it all back by redefining and qualifying opening sentence
Finishing Finesse	Summarizing ideas that were never expressed in order to achieve meandering ending

Many Healthcaremen can get by on these gambits alone. But some insist Healthcaremanship is not as simple as medical writing. Perhaps not. Anyway, for those who wish to further develop their skills, I have come up with these gambits.

Saxon Sidestep
Management Maneuver
Computer Connection
Science Screen
Comprehensive Offensive
Buzz Bomb

Saxon Sidestep

Healthcaremanship is a game of fundamentals. And perhaps the most fundamental thing is this: never use a short word where a long one would do. Short words tend to be Anglo-Saxon in origin. They also tend to be direct and to the point. Since the Healthcareman's aim is to impress and not to inform—to occupy space with dignity while adding nothing new—he should sidestep Saxon expressions. Here are examples.

Saxon	Saxon Sidestep	Gain in Space
use	utilization	8 letters
start	implementation	10 letters
nurse	care coordinator	11 letters, one word
hospital	Health and Allied Sciences Center	24 letters, four words

Management Maneuver

This gambit is far more subtle because it rests on a philosophical assumption—that your opponent knows so little about the arcane art of management that you can baffle him with managerial terms. Managers believe this works particularly well on physicians. The physician, it seems, is capable of making decisions about one person. After all, that's what diagnosis and treatment are about. But he can't grasp decisions that involve many people. That's management.

In any event, the Management Maneuver is a variation of the Double Dawdle. You maneuver the situation (a memo, a committee meeting, a speech, a newspaper release) to the point where a decision must be made involving more than one

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*Reece, R. L.: Space-Occupying Gambits for Medical Writers. J Amer Med Assn, 200:56 1967.

person.

Then you drop a pair of managerial words out of the blue. Why a pair? 1. Because two words are always better than one; and 2. Because you must always qualify a noun. Never let a healthcare word stand alone.

Paired Expressions for Management Maneuver Gambit	Noun Alone #Letters	Noun + Qualifier #Letters	% Gain in Space
Feasibility studies	7	17	+143%
Longterm planning	8	16	+100%
Integrated objectives	10	20	+100%
Coordinated resources	9	20	+122%
Systematic analysis	8	20	+150%

Computer Connection

It is always good gamesmanship for the Healthcareman to show that what he's saying has some connection with computers. The reasons are not hard to find. In the first place, not many people know how computers work. Secondly, computer talk is impressive for its own sake. And thirdly, the computer is a logic machine. Therefore, when you use computer words, what you're saying must be logical:

Any of the following words will do (in any combination):

Adjectives	Nouns
Systematized	Systems
Digital	Programs
Programming	Feedback
Cybernetic	Bits
Binary	Memory
Compatible	Interface

Science Screen

As you might guess, the Science Screen is a good deal like the Computer Connection. You simply try to send up a scientific smoke screen so your opponent will not know what you are saying.

I could give you many examples of words that create this effect, but for reasons of space, I'll settle for one: *Parameter.*

Now there, you'll have to admit, is a word with a scientific ring—a word of precision. But no one, fortunately, knows what it means. Look it up in any dictionary (I have), and you'll find it's a mathematical expression meaning a variable constant which varies with the circumstances of its application. A radius, for example, is a parameter of a circle. Vary the size of the circle, and you vary the radius, even though it remains constant in relation to the circle. A scientific word that means a variable constant is an ideal Science Screen. It should keep your opponents going around in circles.

Comprehensive Offensive

This is probably the most powerful single gambit the Healthcareman has at his command. It powerful for three simple reasons: (1) It has emo tional appeal; (2) It puts the opposing player o the defensive; and (3) You rarely have to defir what you mean.

It's also powerful because it's easy to use. Yo simply pick a word that fits the audience you'r addressing (or the opponent you're toying with and attach any of the following comprehensiv adjectives to the term "Health Care."

Universal
International
Nation
Regional
Community
Local
Total
Comprehensive
Complete
Multiphasic
Organized
Individual

Some of the critics of this gambit have rename it the "Illusive All-Inclusive," "Care Dare," o "Health Stealth." But the critics are just upse because of the gameman's offensiveness. Remem ber. There's no defense against a comprehensiv offensive.

Buzz Bomb

The last gambit I shall describe should only b used in desperation, never indiscriminately.

A few years ago, a member of the U. S. De partment of Agriculture, now forgotten but no gone, first described "buzz words." These word served as bureaucratic bombs. If you were cor nered, you dropped three of them in quick succes sion. You simply arrange your favorite words i three columns—two qualifying adjectives and a abstract noun. Then, if anyone asked you ar embarrassing question, you triggered your buz bombs in 1-2-3 order.

Here, to illustrate the point, are three column of Healthcare buzz words.

1	2	3
total	management	care
regional	supportative	coordinator
universal	health	analyses
primary	integrated	centers
comprehensive	ambulatory	services
national	resource	priorities
quality	pilot	planning
interdependent	involvement	needs
preventive	paramedical	studies
systematized	effectiveness	utilization
feasible	digital	implementations
delivery	scientific	objectives
unmet	outreach	systems
community	allied	maintenance
centralized	medical	parameters
longterm	multiphasic	feedback
		crises

How could you use these lists?

Well, if your opponent is pressing, you can uickly drop *one* 1-2-3 combination, e.g.

"Don't you regard *Centralized Health Needs* as ompulsory?"

That qualifies as a single Buzz Bomb.

But if the opponent counters with: "What do ean by *Centralized Health Needs?*, you assert:

"Centralized Health Needs simply represent *ystematized Health Implementation* in order to btain Quality Health Maintenance."

That statement is a triple Buzz Bomb, or a Buzz litz. To put it even more eloquently, you could all it a Healthcare Blitzkrieg.

If you wish to be more discriminating in your ttack, i.e. to drop "smart" buzz bombs, you may o so far as to define what you mean.

Here, with dogmatic brevity, are a few definitions:

Healthcare Terms	Meaning
Health maintenance examination, preventive health study, systematic review of health systems, interdependent multiphasic health evaluation	Physical Examination
Medical Center, Health Center, Health and Allied Sciences Center, Multiphasic Health Utilization and Implementation Center	Hospital
Ambulatory Food Services, Central Food Processing Center	Cafeteria
Ambulatory Crisis Center, Comprehensive Care Center, Health Crisis Center	Emergency Room
Ambulatory Care Services, Supportative Health Systems, Ancillary Outreach Programs	Outpatient Departments
President, Vice-President, and Corporate Officers for Preventive and Allied Health Maintenance	Hospital Administrators
Primary Resource Nurse	Floor Nurse
Utilization Coordinating Nurse	Head Nurse
Primary Health Care Physician, Total Health Care Physician	General Physician
Uniphasic Physician	Specialist
Health Care Management, Health Care Maintenance, Multiphasic Services and Planning	Diagnosis and Treatment
Multiphasic Analyses, Digitalized Supportative Studies	Laboratory Tests
Delivery of Health Care, Universal Health Care, Health Care Systems	Medicine

Conclusion

Use these gambits often. You'll find them ideal for obtunding sharp-witted opponents. Indeed, if you use these often enough, you may even induce complete cerebral shutdown.

Calendar of Events

December

4—Minneapolis Ophthalmology Society, 12:15 p.m., Central YMCA, Room 104.
5—Abbott Hospital Staff meeting.
5—Unity Hospital Staff Meeting.
6-9—American Rheumatism Association, Pittsburgh Hilton Hotel, Pittsburgh.
7—Minneapolis Surgical Society, Minneapolis Club.
7—Twin Cities Orthopaedic Society, 6:30 p.m., Town and Country Club, St. Paul.
8—Minnesota Academy of Ophthalmology and Otolaryngology.
9—Minnesota Academy of Family Physicians Board of Directors meeting.
11—Hennepin County Academy of Family Physicians Chapter meeting, Minneapolis Athletic Club, Cavalier Room.
12—Eitel Hospital Staff meeting.
12—St. Mary's Hospital Staff meeting, 6:30 p.m., at the hospital. Election.
13—Minnesota Academy of Medicine, Town and Country Club, St. Paul. Dinner meeting. Visitors by invitation.
14—Fairview Hospital Staff meeting, 6:30 p.m., Minneapolis Club.
14—Hennepin County Academy of Family Physicians Executive Committee meeting, 7:30 a.m., Sheraton Ritz Hotel.
18—Minneapolis Academy of Medicine, 6:30 p.m., Minneapolis Club, Visitors by invitation.
19—Fairview-Southdale Hospital Staff meeting, Camelot Restaurant, Jct. 494 and Hwy. 100.
20—Mercy Hospital Staff meeting, 6:30 p.m.
21—Lutheran Deaconess Hospital Staff meeting.
22—Methodist Hospital Staff meeting, 8:00 a.m. Election by mailed ballot.
26—North Memorial Hospital Staff meeting, 6:15 p.m., at the Golden Valley Golf Club.

Alcoholism and Drugs

Addiction

T. G. LARSON, M.D.

ALCOHOL IS BY far the most commonly abused drug in America. However, alcoholics share basic characteristics with all addicts. Actually alcoholics and other drug addicts often change to another agent for various reasons. Most often, withdrawal effects of one agent are countered with the intoxicant effects of another agent. Pep pills are thus used to counter hangover and depression caused by withdrawal effects of sedatives and vice versa. Alcoholics frequently interchange other sedatives such as barbiturates and tranquilizers because they are available and are difficult to detect.

Addiction is the repeated use of a foreign agent to produce a previously experienced mental and physical state. Without this repeated use of the foreign agent the addict becomes anxious and depressed. He may become acutely disturbed emotionally. If the addict cannot obtain his drug at all, he may be in danger of acute withdrawal symptoms which may range from mild muscle cramps to convulsions and death. For the typical addict, his drug gradually becomes the dominant factor controlling his thought and behavior. His "life style" (work, friends, family, health) is determined by his compulsive addiction.

Gradually the addict develops certain characteristics which are generally shared by other addicts regardless of the agent which is used. He is seclusive, secretive and anti-authority in his relationship to other people. He denies that he is "hooked." He rationalizes that he can quit the agent if he really chooses to. He becomes irritable when anyone confronts him with his addicted state. Gradually or abruptly, he sacrifices all interests and responsibilities in order to continue his addiction. Unless his addiction is interrupted, the addict deteriorates mentally and physically to a point of where he suffers permanent damage or death.

The actual conditions and problems seen in addiction depend upon the stage of addiction. Four stages of addiction are described. In each stage the problems for the addict, his family and society are outlined. The actual problems for the individual addict may vary due to age, race and social class.

Dr. Larson is the Medical Director of Northern Pines Mental Health Center, Inc., Little Falls, Minnesota.

Stage 1

The episodic repeated use of the addictive agent. The addict continues to work but misses work due to hangovers now and then. He continues a superficial role in family and society. In this stage the core of addiction is established. The addict begins to use the agent in solitude and to excess without regard for his immediate circumstances. He begins to hide the times and extent to which he uses the agent. Most important, he denies the drug has him "hooked." This denial extends to his own comprehension of his condition.

Addict: Suffers from hangovers, fatigue and depression. Feels guilty about lapses in responsibility, often irritable and preoccupied.

Family: Income lost due to missed work and cost of agent. Marital discord caused by intoxicated states. Children lack carefree, spontaneous interaction with parent. Children see example of meeting problems by denial and resort to drug.

Society: No noticeable direct effect. Later inherits children of the family who may be psychologically deficient and emotionally vulnerable to repetition of parent's addiction.

Stage 2

Addict uses drug almost every day. He misses work, abdicates role in family, curtails social life. Addict at this stage is never free from the disease of addiction. He is constantly in a state of intoxication or in withdrawal misery. A constant acute brain impairment clouds his judgment and his understanding of his condition. He loses control of self regulating abilities and is dependent upon others for constructive decisions. He must be regarded as physically and mentally ill.

Addict: Must use more and more of agent to control withdrawal misery. Alienated from family and friends. Feels isolated and depressed much of the time when he is sober enough to know what his feelings are. Frequently fired from jobs, loses personal esteem. Begins to compro-

mise moral values and responsibility. Denial of problem is solidified.

Family: Continual financial problems. Wife must work if addict is husband. Spouse must build life separate from addict. Children often without parental support and guidance. Addict usually abusive emotionally and physically to family. Family unit borders on collapse.

Society: Loss of stable worker, loss of self-sustaining family unit. Must absorb and maintain children deficient in emotional, moral and responsible attitudes.

Stage 3

Addicts work only sporadically. He is separated from family. He associates with other addicts only. Frequently requires hospitalization and often is in trouble with the law. Gross moral deterioration is evident.

Addict: Mental confusion pervades activities and thought. Agonizing guilt feelings about failures. Feels trapped, physically ill most of the time. Frequently suicidally depressed. Feels totally isolated, making addictive agent his only solace.

Family: Divorced or separated with consequent personal problems to members. On AFDC if father is addict; children in foster homes if mother is addict. Family suffers from society's disfavor and prejudice. Children likely to be school dropouts. They are prone to repeat the parent's distorted relationships and their irresponsibilities.

Society: Must bear cost of supporting addict in hospital or jail plus the cost of family on welfare. Society suffers from insult of crimes by addict such as stealing, burglary, armed robbery, assaults, drunk driving, deaths, etc. Children of addict often untrained and unemployable. They need vocational training and frequently are too disturbed or too irresponsible to support themselves or their families.

Stage 4

Denial of problem is replaced by inability to comprehend the problem. Memory deficit, loss of problem solving ability, and lack of comprehension indicate brain dysfunction and probable permanent brain damage. Addict should be considered psychotic and not responsible for his decisions. If damage is permanent, the addict must be regarded as permanently inadequate to make major decisions for himself. Institutional care is usually mandatory unless and until brain damage is corrected.

Addict: Must endure enforced or voluntary hospitalization indefinitely to save his life. Inability to comprehend his condition further confuses the addict's need for protection from himself.

Family: Hopeless loss of parent and spouse is recognized. Children confused and embarrassed by prolonged hospitalization of parent. Helplessness permeates the family. They are powerless to change their condition. Frequently the family just quits trying. They suffer from loss of self-esteem, guilt feelings, and chronic depression.

Society: Cost of long term hospitalization of addict must be born by taxpayers. Almost impossible to rehabilitate addict due to personality and cerebral deficit. Must absorb children who are handicapped by severe emotional problems and lack of motivation to change.

The basic cause of addiction is unknown. As in most problems where the cause is unknown we find many unproven theories. Without proven facts, anyone's theory about causation is just as good as anyone elses. Actually we may find that there is no single cause.

Whatever the cause, there does seem to be a sequence of events leading to addiction. Addiction often starts in a social setting where the potential addict is introduced to the addicting agent. Into this setting the potential addict brings a subtle antisocial attitude. Specifically this antisocial attitude is a disregard of society's knowledge and attitude towards the dangers of drug abuse. This antisocial attitude sets up the mechanism of denial which is so basic to the addict's personality. It is this denial of a problem which allows him to continue the abuse of the drug.

No matter what the cause of addiction may be, once established the addict seems never to lose the potential to abuse drugs. In a real sense the addict's reflexes and responses may be compared with riding a bicycle. Once the complex reflexes and coordinating movements necessary to ride a bicycle are mastered, these actions become automatic and permanently established. With hardly any conscious effort the person who has not ridden a bicycle for many years can reactivate these pathways and ride a bicycle again. In much the same way once addictive pathways and reflexes are established they seem to be permanently fixed. The addict thus is constantly in danger of reactivating these pathways which constitute addiction.

Present day treatment of addiction is unsatisfactory. Conventional psychiatric treatment is essentially ineffective. Due to his denial of addiction the addict is unmotivated to stop his drug abuse.

The only known effective control of the problem of addiction is to separate the addict from the addictive agent. Drying up the sources of addictive drugs is not practical since most of the drugs abused have a legitimate use for many non-addicts.

Thus, there are only two known ways to control addiction:

1. External restraint of addict from his drug. This is accomplished by institutionalization such as in a hospital. This is costly and only temporarily effective since the addict is not motivated to give up his drug. Relapse into addiction shortly after discharge is the rule rather than the exception.
2. Internal restraint of the addict from his drug. Some addicts retain enough insight to realize that drug abuse is causing most of his current problems. For the addict, to deny himself the drug requires a major change in his life style. He must be motivated sufficiently to undergo a "Conversion" to a life style without drugs. Several group therapy organizations offer assistance to these addicts. Alcoholics Anonymous, Synanon, and the Jesus Movement rely on the mechanism of "conversion" to a lifestyle without drugs. To join these groups the addict must be "converted" to the beliefs and attitudes of the respective groups. The conversion experience gives the addict motivation and a strong reason to change his addictive lifestyle to one without drugs.

Unfortunately, only a small percent of addicts have enough insight and motivation to change. Most addicts deny their problem and thus are untreatable, except by physical separation of the addict from his drug. Usually this means enforced or voluntary institutional care in a hospital, jail and such.

Since treatment of addiction on the whole is unsatisfactory, prevention of the problem seems to be the only practical approach to addiction. Some major changes in society's attitude toward drug abuse must occur. Society should disapprove generally and individually the abuse of all psychoactive chemicals. The "cute" behavior of the drunk should not be viewed with tolerance and acceptance. Movies and television show many scenes where drinking alcohol or taking drugs is commonplace. Children observe the hero and heroine running to the ever present bottle or pill box when they are under pressure. This solution to problems really sets the stage for young people to do likewise when they are under pressure. These practices should be removed from the public media. A stark honest description of addiction and its problems to the addict, his family, and society should be emphasized.

The use of negative advertising has been established in the case of cigarette addiction. Television advertising is now prohibited and has been replaced to some extent by advertisements which discourage cigarette smoking. The law now requires a printed warning that "cigarette smoking is dangerous to health" on each pack of cigarettes.

A similar negative advertising should be demanded for the abuse of drugs and alcohol. Actually the risks to health from the abuse of drugs and alcohol is just as certain as is cigarette smoking.

The potential addict should be confronted with the damage he can do to his family, his friends, and his society as well as to himself. First exposure to drugs today is in the elementary grades. This fact indicates that drug information and drug addiction problems should definitely be presented to children at least by the fifth grade in rural as well as urban areas.

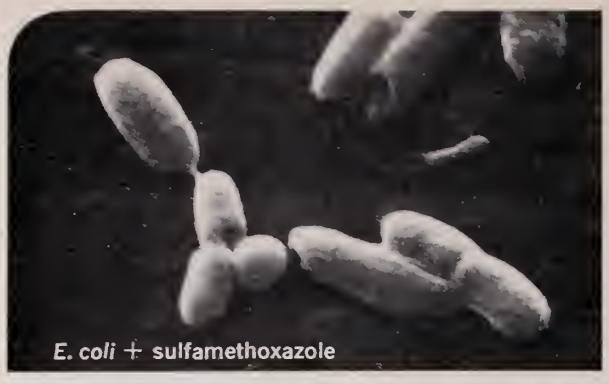
References 1-5 will be found on page 1170.

Encounter under the Scanning Electron Microscope



SEM reveals changes in *E. coli* exposed to antibacterial agents

The Scanning Electron Microscope (SEM) is the only instrument which gives 3-dimensional views on a microscopic level. This permits the surface morphology of microorganisms to be observed in detailed perspective. Changes in surface morphology of *E. coli* exposed to various antimicrobial agents are seen on the following page. An SEM photomicrograph of normal control *E. coli* appears above.









Different modes of antibacterial action — Similar changes in morphology

As part of a series of experiments,[1-3] strains of *E. coli* proven susceptible to each antibacterial agent were exposed to 1 MIC of the respective antibacterials for a three-hour period. Included were cell-wall-active drugs, ampicillin and cephalothin; a drug interfering with intracellular protein synthesis, tetracycline; and a chemical agent which acts by interference with para-aminobenzoic acid, sulfamethoxazole.

As seen above, elongation of the bacilli, mid-cell defects and spheroplast-like forms may be appreciated with the SEM technique. These changes in bacterial morphology were similar . . . regardless of the antibacterial agent used and irrespective of its mechanism of action.

"At present, the significance of these observations in clinical infection must be considered with caution, but it is hoped that these data will stimulate a reevaluation of present concepts of the nature and role of morphological variants of bacteria exposed to a variety of antibacterial factors."[2]

It should be noted that no clinical conclusions can be drawn from this study, as it is not always possible to extrapolate *in vitro* data to humans.

References: 1. Klainer, A. S.; Fass, R. J., and Perkins, R. L.: Scientific Exhibit presented at the 25th American Medical Association Clinical Convention, New Orleans, La., Nov. 28-Dec. 1, 1971. **2.** Klainer, A. S., and Perkins, R. L.: *Antimicrob. Agents Chemother., 1*:164, 1972. **3.** Klainer, A. S.: Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A [illegible] hemolytic streptococcal infections and will not eradicat[illegible] prevent sequelae (rheumatic fever, glomerulonephritis) of [illegible] infections. Deaths from hypersensitivity reactions, agranulo[illegible] sis, aplastic anemia and other blood dyscrasias have bee[illegible] ported and early clinical signs (sore throat, fever, pallor, pur[illegible] or jaundice) may indicate serious blood disorders. Frequent [illegible] and urinalysis with microscopic examination are recommen[illegible] during sulfonamide therapy. Insufficient data on children u[illegible] six with chronic renal disease.

Precautions: Use cautiously in patients with impaired [illegible] or hepatic function, severe allergy, bronchial asthma; in gluc[illegible] 6-phosphate dehydrogenase-deficient individuals in whom [illegible] related hemolysis may occur. Maintain adequate fluid intal[illegible] prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocyt[illegible]

Encounter in Clinical Practice

Control of primary bacterial offenders

Antibacterial Gantanol® (sulfamethoxazole) controls susceptible strains of *E. coli* and other gram-negative and gram-positive organisms often implicated in acute nonobstructed pyelonephritis and cystitis.

Prompt antibacterial blood and urine levels

In from 2 to 3 hours after the initial 2-Gm adult dose, antibacterial levels are present in both the blood and urine.

B.I.D./T.I.D. dosage for around-the-clock coverage

Subsequent 1-Gm doses provide up to 12 hours of antibacterial coverage. More severe u.t.i. may require a q. 8 h. dosage regimen. Either schedule provides coverage during the waking and sleeping hours—especially important during hours of sleep when normal urinary retention tends to favor bacterial proliferation.

Also effective in nonobstructed chronic and recurrent u.t.i.

It is not uncommon for the elderly and the debilitated to develop chronic and/or recurrent nonobstructed urinary tract infections such as pyelonephritis and cystitis. Such cases often respond satisfactorily to Gantanol. The increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents including sulfonamides, especially in chronic or recurrent u.t.i.

Your Option: Tablets or Suspension

Either dosage form—the Tablets or the pleasant-tasting, cherry-flavored Suspension—can provide the dependable antibacterial activity necessary to control susceptible nonobstructed cystitis and pyelonephritis. Symptomatic improvement may usually be expected in 24 to 48 hours. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake. Gantanol (sulfamethoxazole) is generally well tolerated with relative freedom from complications; the most common side effects are nausea, vomiting and diarrhea. Frequent c.b.c.'s and urinalyses with microscopic examination are recommended.

In nonobstructed cystitis and pyelonephritis due to susceptible organisms

Gantanol®
(sulfamethoxazole)
Basic Therapy

---

astic anemia, thrombocytopenia, leukopenia, hemolytic ane-
, purpura, hypoprothrombinemia and methemoglobinemia);
rgic reactions (erythema multiforme, skin eruptions, epider-
necrolysis, urticaria, serum sickness, pruritus, exfoliative
matitis, anaphylactoid reactions, periorbital edema, conjunc-
l and scleral injection, photosensitization, arthralgia and
rgic myocarditis); *gastrointestinal reactions* (nausea, emesis,
ominal pains, hepatitis, diarrhea, anorexia, pancreatitis and
natitis); *CNS reactions* (headache, peripheral neuritis, men-
depression, convulsions, ataxia, hallucinations, tinnitus, ver-
and insomnia); *miscellaneous reactions* (drug fever, chills,
c nephrosis with oliguria and anuria, periarteritis nodosa and
phenomenon). Due to certain chemical similarities with
e goitrogens, diuretics (acetazolamide, thiazides) and oral
oglycemic agents, sulfonamides have caused rare instances
goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Enclosed is my check for $_____
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Fracture Conference

Care of Fractured Hip in the Aged

ELI J. KRIGSTEN, M.D., PETER L. BOMAN, M.D. AND EINER W. JOHNSON, JR., M.D.

Eli J. Krigsten, M.D.:

As an orthopedic problem, fracture of the hip in an elderly person presents several facets not apparent in younger patients. These have been covered in several good articles.[1-7] The mortality and the morbidity rates have varied somewhat from series to series. Niemann and Mankin[1] recently noted that 36% of the patients died within six weeks after operation, with the peak incidence in the second week. Of the remaining patients in the group who were ambulatory before operation, only 20% ever walked again. Niemann and Mankin believed that age and wound infection were the major causes of death and that the type of fracture, operative technique, and duration of anesthesia were not significant in this respect.

In the series of Manpel and colleagues[4] the mortality rate was less if the fracture was more distal: 13.2% after subcapital fracture and only 4.1% after subtrochanteric fracture. Fitts and colleagues[7] stated: "The life expectancy of the patient who survived the first six months after operation was not appreciably less than the general population." They too found greater mortality and morbidity after intertrochanteric fracture than after neck fracture. Among the survivors, however, 97% of those with intertrochanteric fracture had a good result, avascular necrosis occurring in only 13%.

A major influence in the survival of Niemann and Mankin's[1] patients was major wound infection, which occurred in almost 20% and was especially common in patient with prostheses. Circumstances possibly causative were lack of foreskin cleanliness, poor bowel and bladder control, poor inherent hemostasis, and a nebulous condition they called "poor resistance." All the femoral-head prostheses in their series were inserted through a Fletcher-Marcy (posterior) incision which was not routinely drained and was easily soiled by excretions.[1]

Fracture Conference, April 28, 1969.
Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

We have dealt recently with hip fractures in some elderly patients at the Rochester State Hospital whose pyschiatric difficulties made special problems. To get them to walk as soon as physically possible was hard, since many could not understand simple instructions. Parkinson's disease was an added handicap in some cases. In the Oltman series,[5] made up of psychiatric patients in Connecticut, the peak incidence of fracture occurred in the eighth decade of life, the average age being four years less among men than among women. Some patients fell because of ataxia. In 1960, Sheldon of England described what he called a "drop" attack, intimating that about one fourth of all falls by the aged occurred for no apparent reason. Oltman and Friedman[5] believed hip fractures caused higher mortality and greater incidence of degenerative conditions (especially cardiovascular and renal) in psychiatric patients than in others. In the 74 autopsied cases, the most frequent cause of death was bronchial pneumonia.

These statistical studies suggest that hip fracture is a lethal condition. Most authorities agree that internal fixation within three days after the injury produces the best survival rates. In Bickel and Jackson's[2] series of intertrochanteric fractures, the average time elapsing before internal fixation was two days and the mortality rate was approximately 8%, which is lower than the rates in most other large series.

The fortunate results we have been able to obtain on our service are due primarily to our medical colleagues, who cooperated in preoperative evaluation and care. The selection and administration of anesthetics and the help of our respiratory service have also been important. In addition, we have been using anticoagulants prophylactically, beginning usually on the third postoperative day and continuing until the patient either is actively ambulating or is dismissed.

Peter L. Boman, M.D.:

Preoperative evaluation of an elderly patient is

just as important as proper selection of surgical approach or postoperative care. The patient's history should be carefully reviewed. One should ask especially about the cardiovascular, respiratory, and metabolic systems and about intercurrent diseases. It is important to make a careful physical examination, if this is possible. An evaluation of mental function will make it possible to assess any future changes. And finally, adequate laboratory examinations, including electrocardiography, are needed.

Such an extensive examination will usually answer the question: When is the patient best able to tolerate anesthesia and surgery? McLaughlin believed that the time of injury was best and that such injuries should be considered surgical emergencies. Contraindications are congestive heart failure, cardiac arrhythmia, and diabetic acidosis. Lipscomb,[6] however, believed that these are not surgical emergencies and recommended that operation be performed when the internist, anesthesiologist, and surgeon agree that the time is ripe.

Dr. Kimmel:

For orthopedic anesthesia, the aged are a most difficult group. One major improvement has been the change from the concept that hip surgery is an emergency. There is an optimal time: not immediately and not a week later, but perhaps within 24 hours or at least within three days.

The choice of anesthesia is not simple and usually has to be made with cooperation between the surgeon and the anesthesiologist. A difficult fracture may take three or four hours, thus exceeding the duration of spinal anesthesia. Also, under general anesthesia the patient with respiratory problems can be ventilated well; often his condition is better at the end of surgery than at the start. Although there are problems with spinal anesthesia, I prefer to use this method when I can. The major problem is getting the patient in position to receive it, because he frequently has a lot of pain. Another problem is that spinal anesthesia predisposes to hypotension, which is bad for these patients. They have limited coronary reserve, and hypotension often contributes to their early death.

Another method is local infiltration, which we have recently used in two extremely poor-risk patients with good results. So there is no easy answer, nor any one way to handle these patients. The choice depends largely on the patient's condition and on the surgeon's and anesthesiologist's combined judgment.

Dr. Krigsten:

We have operated on several elderly fracture patients under spinal anesthesia and on one under local anesthesia. He had pulmonary fibrosis and was not a candidate for general anesthesia. The local anesthesia worked well and the patient did well.

Dr. Cabanela:

I present the case of an 82-year-old woman who fractured her right hip in a fall at home. The past medical history included severe kyphoscoliosis with decreased chest expansion arteriosclerotic heart disease with mitral insufficiency, and a fracture of the left hip sustained 15 years previously. The fracture of the right hip was openly reduced and internally fixed. The roentgenogram made on admission is shown in Figure 1.

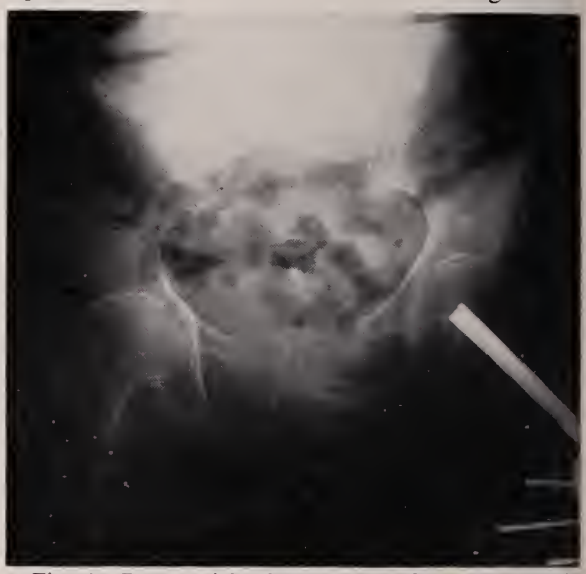


Fig. 1—Recent right femoral-neck fracture and old left femoral-neck fracture.

Dr. Krigsten:

Her left hip had healed nicely. Although the fracture does not show well, it is situated distally in the femoral neck. Her kyphoscoliosis was so severe that she was bent almost to a 90° angle. Her size and her spinal deformity presented a real problem in positioning her for operation and in doing it. The fixation we were able to obtain is shown in Figure 2. Some articles have described the backing out of the Smith-Peterson nail in this type of fracture. For insurance, therefore, I inserted a Knowles pin beside the V-blade plate. She was ambulating with a walker two weeks after operation.



Fig. 2—Same patient as in Figure 1. Recent, right femoral-neck fracture internally fixed with V-blade plate and one Knowles pin.

Dr. Cabanela:

The next patient is an 86-year-old man who woke up one morning recently with pain in the right hip aggravated by any motion of the lower extremity. He was brought to the emergency room, where the roentgenograms shown in Figure 3 were taken.

Dr. Krigsten:

This man came in a semicomatose condition. Figure 4 shows our fixation. We used four Knowles pins and, although we thought we had put them in a diamond pattern, they do not appear so on this roentgenogram. He did well postoperatively; and on dismissal he was lucid, talking, and ambulating with crutches. His post-



Fig. 4—Same patient as in Figure 3. Right femoral-neck fracture internally fixed with four Knowles pins, as seen at time of operation.

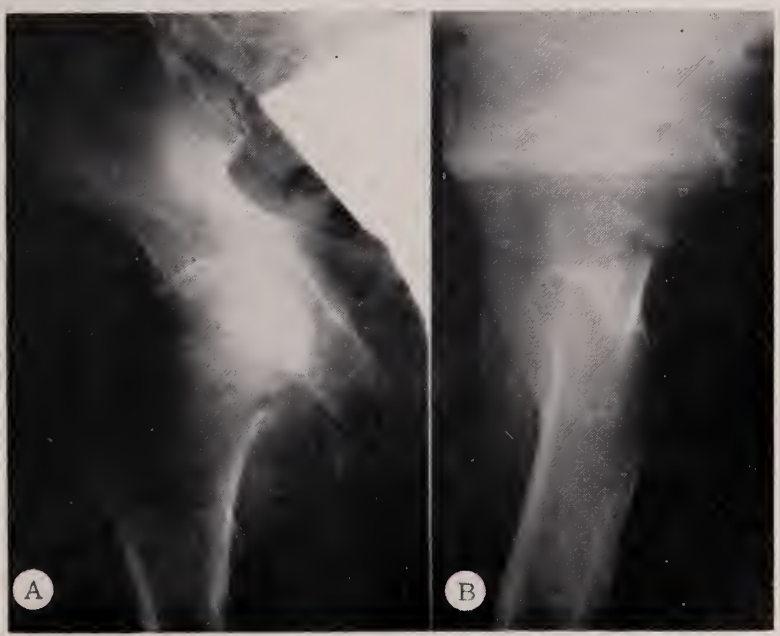


Fig. 3—Right femoral-neck fracture. *(A)* Anteroposterior view. *(B)* Lateral view.

operative care was certainly enhanced by the help we got from the respiratory service.

Dr. Cabanela:

A 69-year-old woman fell at a nursing home during a dizzy spell, sustaining an injury to the right wrist and the right hip and lacerations of the scalp. On arrival in the emergency room she was not alert. She had good peripheral pulses and a typical deformity of the fractured hip. The past history included severe long-standing Parkinson's disease, marked osteoporosis, two previous episodes of syncope, and fracture of the left hip treated here with a Matchett-Brown prosthesis in July 1968.

Dr. Krigsten:

This woman had two hip fractures within a year. At a fracture conference a couple of years ago we discussed whether we should attempt to nail fractures of the femoral neck in patients with Parkinson's disease. I think it is generally conceded that this is not the best course. Insertion of a primary prosthesis is best, if age will allow it. The wrist fracture hindered use of crutches, and progress was rather slow; but the patient was using a walker by the time she left the hospital.

One last comment is that often we take a somewhat aloof attitude because these patients are old and debilitated and nobody welcomes the many problems they present. But a little time spent in perhaps just patting their hands and combatting their depression may be worthwhile. It is gratifying to see an elderly person walk out of the hospital after sustaining a hip fracture, which can be a lethal injury.

Summary

Let me make these points: (1) Appropriate and complete preoperative evaluation of the elderly patient is essential to proper fracture care. (2) Operation on these patients should not be done as an emergency, but probably should not be delayed more than three days except in dire circumstances. (3) The type of anesthesia is important. The anesthesiologist will be of prime help in selecting the proper type and should be asked to see the patient preoperatively. (4) Internal fixation of the fracture is the best treatment, where possible, and allows early mobilization.

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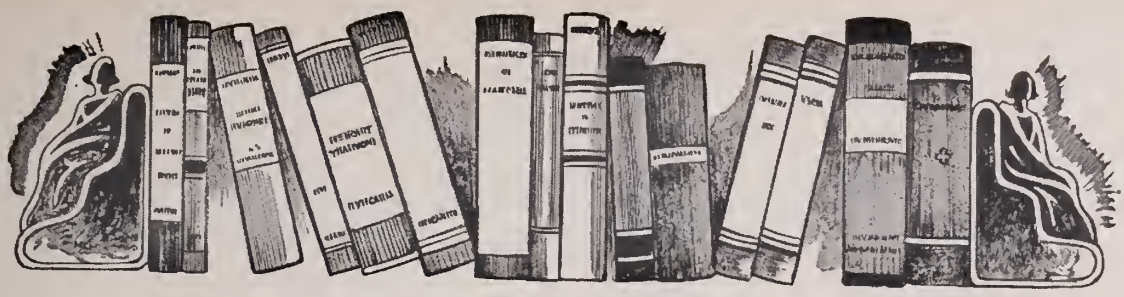
Dr. Spink to Write History of Infectious Diseases

Dr. Wesley Spink, Regents' Professor of Medicine and Comparative Medicine at the University of Minnesota, has been awarded a $77,000 project grant by the Department of Health, Education and Welfare. Dr. Spink, who will retire June 30, 1973, plans to trace the evolution in the scientific control of infectious diseases.

Results of Spink's three-year project, which will begin July 1, 1973, will be published in a comprehensive monograph presenting historical highlights in the control of infectious diseases, details of outstanding advances and discussion of progress and problems of the future in this field.

The volume is planned in five parts: the 19th century; the first two decades of the 20th, including a review of medical knowledge and control of infectious diseases at the end of World War I; the period from 1920 to 1937 (during which Spink began his career as a student of infectious diseases); 1937 to 1970, a period encompassing World War II, and marked by more advances in the specific therapy of disease than at any time in medical history; and a forecast of future developments in the control of infectious diseases.

The volume will be published by the University of Minnesota Press.



Book Reviews

FRONTIERS IN COMPARATIVE MEDICINE by W. I. B. Beveridge. Published by the University of Minnesota Press, 1972. 104 pages. Price $4.95

This volume is subtitled "The Wesley W. Spink Lectures on Comparative Medicine, Volume 1" suggesting that the University of Minnesota Press will publish subsequent volumes as this biennial lectureship continues.

The first series of lectures was a peripatetic affair with W. I. B. Beveridge, Professor of Animal Pathology at the University of Cambridge, England, speaking at Carleton College, University of Minnesota-St. Paul and University of Minnesota-Duluth. The three lectures comprise the three chapters of this book. The first is "Logic of the Comparative Method" in which Beveridge explores the application of comparative medicine to human medicine. The second chapter, "Animal Model of Human Diseases" is concerned with the development of the great scientific programs of animal investigation in medical schools. And the third chapter "Comparative Study of Influenza" is a fascinating account of this most important epidemic disease as it has scourged the world in epidemics in recent centuries.

The choice of Beveridge to lead off this series of Spink lectures is a happy one. He presents this material so important in infectious disease in a way that expands the physician's horizon of interest far beyond the care of human patients.

This volume is a model of perfection in translating a series of lectures into book form. We look forward to further contributions in the Spink Lectureship Series.

Reuben Berman, M.D.
Editor

GENERAL UROLOGY by Donald R. Smith, M.D. Lange Medical Publications. Price: $8.50.

For a long time General Urology has been a fine urological textbook for medical students and a valuable reference for internes and general practitioners. Dr. Smith wrote the entire book himself except for five of the 31 chapters. The author has revised and updated all of the chapters in this new seventh edition. Never before has so much information been packed into such a compact volume with so little repetition. After each subject is discussed, the author lists a few of the important references. The book is well illustrated, and the text is printed on a double-column page for easier reading.

General Urology is a compendium of urological disorders, especially as they relate to the different genitourinary organs. Throughout the book the author stresses anatomy, embryology, pathophysiology, diagnostic techniques and differential diagnosis of genitourinary disorders. Although therapy is not discussed in detail, the initial and basic treatment of each disorder is presented in an excellent manner.

A number of diagnostic pearls are offered. For example, in Chapter 4, Dr. Smith describes an extremely valuable technique to aid in the diagnosis of abdominal masses in infants; namely, transillumination of the mass using a fiber optic light cord. The author also inserted chapters which are traditionally not included in most urological textbooks. Chapter 5 on Urologic Laboratory Examination, Chapter 9 on Instrumental Examination of the Urinary Tract, and Chapter 27 (Skin Diseases of the External Genitalia) are important additions.

Because General Urology is a compendium, it is understandable that certain subjects could not be discussed in greater detail. However, I would suggest expanding the section on treatment of uremia in Chapter 10, using higher doses of steroids than those recommended by the author for treatment of shock accompanying gram-negative bacteremia (Chapter 12), and adding a section on genitourinary blastomycosis in Chapter 13 (Specific Infections of the Urinary Tract).

I originally believed that General Urology was written specifically for medical students, internes, and practitioners other than urological surgeons. After reviewing this book, I would also recommend it for urological residents. It is a required textbook for Urological Assistant Trainees at our hospital, the Veterans Hospital.

Clyde E. Blackard, M.D.
Minneapolis, Minnesota

REVIEW OF MEDICAL PHARMACOLOGY by F. H. Meyers, E. Jawetz and A. Goldfien. Lange Medical Publications.

Intended as a comprehensive review of biochemistry for the medical student and practicing physician, Drs. Meyers, Jawetz and Goldfien have prepared a text entitled, "Review of Medical Pharmacology." Its paper back printing permits a price that will appeal to everyone. The chapter headings are handled in the traditional text book fashion.

Although authors have written individual chapters in the text, there is clearly a uniform style. The Table of Contents demonstrates the comprehensiveness of the book. The style is readable, the diagrams and tables are printed well and clearly. This book can be recommended as a shelf reference for all concerned with the subject of molecular biology.

Obviously, however, the moment a book of this nature is printed, the text must yield to the cutting edge of advances in the field.

Robert Maslansky, M.D.
Minneapolis, Minnesota

In gram-negative sepsis..



*Due to susceptible organisms

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See Clinical Considerations section which follows...

The antibiotic to start with...

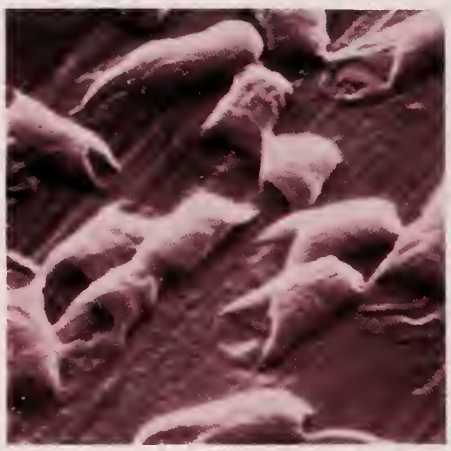
*In suspected or documented gram-negative sepsis due to susceptible organisms, GARAMYCIN Injectable may be considered as initial therapy. T decision to continue therapy with this drug should be based on the results o susceptibility tests, the severity of the infection, and the important concept contained in the Warning Box below.

An indispensable spectrum for today[1-3]

GARAMYCIN Injectable offers a high probability of effectiveness against virtually all of the gram-negative pathogens which are a growing cause of clinical concern. GARAMYCIN Injectable has also demonstrated striking activity against *Proteus* species, both indole-positive and indole-negative.[2]

Proven clinical efficacy[1,4-13]

GARAMYCIN Injectable may be lifesaving in septicemia... may give a dramatic response in wounds and burns complicated by sepsis. GARAMYCIN Injectable has also demonstrated outstanding results in serious gram-negative infections other than sepsis, such as serious respiratory infections and selected urinary tract infections. To date, GARAMYCIN Injectable has been the subject of more than 1,500 published papers and 12 international symposia.





Note: The photomicrographs of gram-negative organisms reproduced here were obtained by a relatively new process employing a scanning beam electron microscope. The pathogens represented are *Klebsiella pneumoniae, Escherichia coli,* and *Proteus mirabilis.* The colors shown here are an artist's representation. The magnification is 10,000X.



WARNING: Patients treated with GARAMYCIN Injectable should be u close clinical observation because potential toxicity associated with use of this drug.

Ototoxicity, both vestibular and auditory, can occur in patients, pr those with pre-existing renal dam treated with GARAMYCIN Injectabl usually for longer periods or with doses than recommended.

GARAMYCIN Injectable is potent

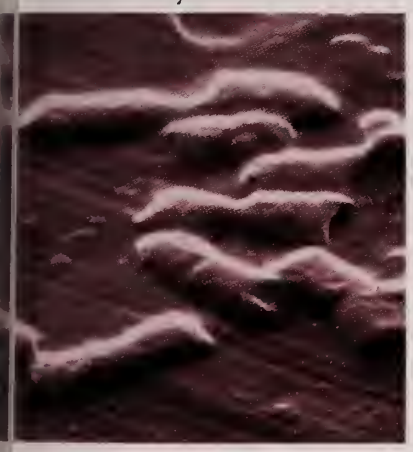
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A high degree of sensitivity maintained[14-16]

Bacterial resistance to GARAMYCIN Injectable has not been a problem to date. In the laboratory, resistance has been demonstrated to develop slowly in stepwise fashion. No one-step mutations to high resistance have been reported. One investigator noted: "In the experience so far with [gentamicin], which is 7 or 8 years, in centers where it's been restricted to parenteral use, resistance has not appreciably changed."[14] Another authority "...found very little emergence of resistance" during eight years of use.[15]

In a survey of published studies on resistance to gentamicin, Weinstein and co-workers[16] report little change in bacterial sensitivity since 1963 in the percentage of sensitive strains. *In vitro* sensitivity was determined in all cases by the tube-dilution method.



Relatively low incidence of adverse reactions[3,14,17]

As with certain other aminoglycoside antibiotics, ototoxicity (primarily vestibular with gentamicin) and potential nephrotoxicity are risks of therapy.

Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy.

In contrast to kanamycin, neomycin, and streptomycin, which primarily cause deafness or difficulties in the auditory end organs of the eighth nerve, gentamicin primarily causes labyrinthian dysfunction.[14] This dysfunction, manifested by dizziness (not deafness) has, in most cases, been transitory.

As to nephrotoxicity, according to Finland,[3] "as in the case of kanamycin, the nephrotoxicity was found to be largely 'potential,' and very little if any has been encountered except with obviously excessive doses or in patients with already damaged kidneys."

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hrotoxic, and this should be kept in d when it is used in patients with existing renal impairment.

fonitoring of renal and eighth nerve ction is recommended during therapy atients with known impairment of al function. This testing is also mmended in patients with normal al function at onset of therapy who elop evidence of nitrogen retention reasing BUN, NPN, creatinine or uria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

Usage in Pregnancy: Safety for use in pregnancy has not been established.

See Clinical Considerations section which follows...

When preculture signs point to gram-negative sepsis...

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For Parenteral Administration

WARNING: Patients treated with GARAMYCIN Injectable should be under close clinical observation because of the potential toxicity associated with the use of this drug.

Ototoxicity, both vestibular and auditory, can occur in patients, primarily those with pre-existing renal damage, treated with GARAMYCIN Injectable, usually for longer periods or with higher doses than recommended.

GARAMYCIN Injectable is potentially nephrotoxic, and this should be kept in mind when it is used in patients with pre-existing renal impairment.

Monitoring of renal and eighth nerve function is recommended during therapy of patients with known impairment of renal function. This testing is also recommended in patients with normal renal function at onset of therapy who develop evidence of nitrogen retention (increasing BUN, NPN, creatinine or oliguria). Evidence of ototoxicity requires dosage adjustments or discontinuance of the drug.

In event of overdose or toxic reactions, peritoneal dialysis or hemodialysis will aid in removal of gentamicin from the blood.

Serum concentrations should be monitored when feasible and prolonged concentrations above 12 mcg./ml. should be avoided.

Concurrent use of other neurotoxic and/or nephrotoxic drugs, particularly streptomycin, neomycin, kanamycin, cephaloridine, viomycin, polymyxin B, and polymyxin E (colistin), should be avoided.

The concurrent use of gentamicin with potent diuretics should be avoided, since certain diuretics by themselves may cause toxicity. In addition, when administered intravenously, diuretics may cause a rise in gentamicin serum level and potentiate neurotoxicity.

USAGE IN PREGNANCY Safety for use in pregnancy has not been established.

INDICATIONS GARAMYCIN Injectable is indicated, with due regard for relative toxicity of antibiotics, in the treatment of serious infections caused by susceptible strains of the following microorganisms:

Pseudomonas aeruginosa, Proteus species (indole-positive and indole-negative), **Escherichia coli** and **Klebsiella-Enterobacter-Serratia** species.

Clinical studies have shown GARAMYCIN Injectable to be effective in septicemia and serious infections of the central nervous system (meningitis), urinary tract, respiratory tract, gastrointestinal tract, skin and soft tissue (including burns).

Bacteriologic tests to determine the causative organisms and their susceptibility to gentamicin should be performed.

Bacterial resistance to gentamicin develops slowly in stepwise fashion; there have been no one-step mutations to high resistance.

In suspected or documented gram-negative sepsis, GARAMYCIN may be considered as initial therapy. The decision to continue therapy with this drug should be based on the results of susceptibility tests, the severity of the infection, and the important additional concepts contained in the "Warning Box." In the neonate with suspected sepsis or staphylococcal pneumonia, a penicillin type drug is usually indicated as concomitant antimicrobial therapy.

GARAMYCIN Injectable has been shown to be effective in serious staphylococcal infections. It may be considered in those infections when penicillins or other less potentially toxic drugs are contraindicated and bacterial susceptibility testing and clinical judgment indicate its use.

CONTRAINDICATIONS A history of hypersensitivity to gentamicin is a contraindication to its use.

WARNINGS (See "Warning Box.")

PRECAUTIONS Neuromuscular blockade and respiratory paralysis have been reported in the cat receiving high doses (40 mg./kg.) of gentamicin. The possibility of these phenomena occurring in man should be considered if gentamicin is administered to patients receiving neuromuscular blocking agents such as succinylcholine and tubocurarine.

Treatment with gentamicin may result in overgrowth of nonsusceptible organisms. If this occurs, appropriate therapy is indicated.

ADVERSE REACTIONS

Nephrotoxicity: Adverse renal effects, as demonstrated by rising BUN, NPN, serum creatinine and oliguria, have been reported. They occur more frequently in patients with a history of renal impairment treated with larger than recommended dosage.

Neurotoxicity: Adverse effects on both vestibular and auditory branches of the eighth nerve have been reported in patients on high dosage and/or prolonged therapy. Symptoms include dizziness, vertigo, tinnitus, roaring in the ears and hearing loss.

Numbness, skin tingling, muscle twitching, and convulsions have also been reported.

Note: The risk of toxic reactions is low in patients with normal renal function who do not receive GARAMYCIN Injectable at higher doses or for longer periods of time than recommended.

Other reported adverse reactions, possibly related to gentamicin, include increased serum transaminase (SGOT, SGPT), increased serum bilirubin, transient hepatomegaly, decreased serum calcium; splenomegaly, anemia, increased and decreased reticulocyte counts, granulocytopenia, th[rombo]cytopenia, purpura; fever, rash, itching, urticaria, generalized b[ron]joint pain, laryngeal edema; nausea, vomiting, headache, increased [sa]tion, lethargy and decreased appetite, weight loss, pulmonary fi[bro]hypotension and hypertension.

DOSAGE AND ADMINISTRATION GARAMYCIN Injectable may be given [intra]muscularly or intravenously.

For Intramuscular Administration:

PATIENTS WITH NORMAL RENAL FUNCTION*

Adults: The recommended dosage for GARAMYCIN Injectable for pa[tients] with serious infections and normal renal function is 3 mg./kg./day, a[dmin]istered in three equal doses every 8 hours.

For patients weighing over 60 kg. (132 lb.), the usual dosage is 8 [mg.] (2 cc.) three times daily. For patients weighing 60 kg. (132 lb.) or les[s] usual dose is 60 mg. (1.5 cc.) three times daily.

In patients with life-threatening infections, dosages up to 5 mg./kg [day] may be administered in three or four equal doses. This dosage shou[ld be] reduced to 3 mg./kg./day as soon as clinically indicated.

*In children and infants, the newborn, and patients with impaired [renal] function, dosage must be adjusted in accordance with instruction[s set] forth in the Package Insert.

For Intravenous Administration:

The intravenous administration of GARAMYCIN Injectable is re[com]mended in those circumstances when the intramuscular route is not [feasi]ble (e.g., patients in shock, with hematologic disorders, with severe b[urns], or with reduced muscle mass).

For intravenous administration, in adults, a single dose of GARAM[YCIN] Injectable may be diluted in 100 or 200 cc. of sterile normal saline [or] a sterile solution of dextrose 5% in water; in infants and children [the] volume of diluent should be less. The concentration of gentamicin in [solu]tion, in both instances should normally not exceed 1 mg./cc. (0.1%) [and the] solution is infused over a period of 1 to 2 hours.

The recommended dose for intravenous administration is identic[al to] that recommended for intramuscular use.

GARAMYCIN Injectable should not be physically pre-mixed with [other] drugs, but should be administered separately in accordance with the [rec]ommended route of administration and dosage schedule.

HOW SUPPLIED GARAMYCIN Injectable, 40 mg. per cc., 2 cc. mult[iple]-dose vials for parenteral administration.

Also available, GARAMYCIN Pediatric Injectable, 10 mg. per cc., [2] cc. multiple-dose vials for parenteral administration. APRIL, '[72]

AHFS Category 8:[12]

For more complete prescribing details, consult Package Insert or P[hysi]cians' Desk Reference. Schering literature is also available from [a]Schering Representative or Professional Services Department, Schering Corporation, Kenilworth, New Jersey 07033.

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Review

Drugs in the Treatment of Cancer

A Review

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Many patients with disseminated cancer can be treated effectively with drugs: for cure in some cases, for prolonged survival in others, and for significant palliation in many. The concept is no longer new; some of these drugs, such as nitrogen mustard, have been in use for a long time while others continue to be developed. In the past few years theoretical considerations have led to new approaches in terms of combination therapy, some of which have been outstandingly successful such as in acute leukemia, Hodgkin's disease, and other lymphomas. It is being tried in several solid tumors as well. Steroid hormone treatment for cancers of the breast, prostate, and endometrium continues to be very important.

Anticancer Drugs

Anticancer drugs are generally divided into two main groups: chemotherapeutic agents and hormonal agents. This discussion is devoted principally to the chemicals of which there are now about 20 in general use. These are divided according to their chemistry and mode of action into four main groups: the alkylating agents, the antimetabolites, the antitumor antibiotics, and the vinca alkaloids. These chemicals act on tumor cells in different ways. The alkylating agents attack DNA directly, whereas the antimetabolites interfere in pathways of DNA synthesis. The antitumor antibiotics may have aspects of both of these actions. The vinca alkaloids are known to interfere with the mitotic process by effects on the mitotic spindle but probably also have another mode of antitumor action.

The majority of the anticancer chemicals have been in use for many years. The oldest, nitrogen mustard, first underwent clinical trials in 1942 although it was not reported in the literature until after World War II. Other alkylating agents, thiotepa, busulfan (Myleran), chlorambucil (Leukeran), cyclophosphamide (Cytoxan), and melphalan (Alkeran), were developed from the mid-1950's to the mid-1960's.

Methotrexate was among the first of the antimetabolites in use (1948) and was followed by 6-mercaptopurine (Purinethol), 5-fluorouracil, hydroxyurea (Hydrea), and cytosine arabinoside (Cytosar).

The first of the antibiotics with antitumor activity used extensively was actinomycin-D (Cosmegen) beginning in 1952-53. This was followed by Mithramycin and now by three other important antibiotics still available for investigative use only but probably to be released soon. These include: Daunomycin used in acute leukemia, Adriamycin undergoing trials in sarcomas and some other tumors, and Bleomycin, developed by the Japanese, effective in certain squamous cell cancers.

The vinca alkaloids, represented by Velban and vincristine (Oncovin) were first reported in 1962-63.

In addition to these major groups, there are other drugs which do not fit conveniently into the above classifications. They include L-Asparaginase, an enzyme prepared from e. coli which is useful in the treatment of lymphoblastic leukemia, procarbazine (Matulane), a drug useful in Hodgkin's disease, and the nitrosoureas, 1, 3-Bis (2-Chloroethyl)-1-Nitrosourea (BCNU) and 1-(2-Chloroethyl) - 3 - Cyclohexyl - 1 - Nitrosourea (CCNU), which probably act like alkylating agents, penetrate the blood brain barrier in contrast to the other known antitumor agents, and have been somewhat useful in glioblastomas. They also have been used in treatment of melanoma and lymphomas.

Although most of these drugs have been in use for years, many physicians have had little experience with them. This may be because of questions of their effectiveness, concern about their toxicity, or lack of information about how to use them—which drug for which tumor, dosage schedules, etc.

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Effectiveness is, of course, a valid concern, because admittedly few tumors are cured, but even in those cases where the known chances for response are small, most patients willingly take that chance. If it does nothing else, it gives them something for which to hope and perhaps a new lease on life, even though short-term.

With regard to toxicity, good responses are frequent enough to justify the risk, but the physician must make every effort to avoid intolerable toxicity and to warn patients about the possibility and nature of side-effects before treatment is started. Inadequate dosage which never produces toxicity may also never produce any clinical benefit. The therapeutic skill is in knowing how to push dosage to obtain maximum benefit and at the same time avoid intolerable toxicity.

Toxicity may be influenced by many factors, among them being the patient's general condition, age, and the amount of previous treatment. Elderly patients generally tolerate less drug, and patients in poor nutritional status with low plasma proteins, impaired liver function, etc., may be very poor risks. Patients who have had intensive prior radiation or chemotherapy also need to be treated very carefully in chemotherapy programs.

It is essential that patients on any of these agents be seen frequently, evaluated for possible toxic symptoms, and have their blood counts checked. This may be weekly or more often in intensive treatment programs; but, later, when dosage schedules have been established, it may be at two to three week intervals but rarely longer.

Specific Drug Toxicities

Cytoxan

The most common serious manifestation of Cytoxan toxicity is bone marrow depression, primarily leukopenia, and, although more platelet-sparing than other alkylating agents, the platelets also may be depressed by Cytoxan. Patients must be warned about the probability of hair loss which occasionally is severe. Actually this may occur with virtually any of the anticancer chemicals but is almost certain when Cytoxan and vincristine are given together. A not very common, but troublesome, side-effect of Cytoxan is hemorrhagic cystitis. To minimize this, it is important that patients on Cytoxan maintain a good fluid intake and output, and it is advisable to give dosage early in the day rather than at night when the offending excretion products may remain in the bladder overnight. Given intravenously, Cytoxan may cause nausea and vomiting.

5-fluorouracil

5-FU also causes bone marrow depression and it is important, as it is with all the chemotherapeutic agents, to check blood counts and platelet counts at regular intervals. Two common toxic reactions to watch for with 5-FU are diarrhea and cheilitis-stomatitis with small ulcerations most often at the mucocutaneous border of the lips. An occasional patient just does not tolerate 5-FU well and feels generally ill for two to three days after each dose. This may be unpleasant enough so that the drug has to be discontinued. An unusual, but quite rare, side-effect of 5-FU is a form of cerebellar ataxia which is reversible after cessation of the drug.

Vincristine

Vincristine causes little bone marrow depression in conventional doses; its main toxic effect is neurological. The earliest symptoms are paresthesias followed by loss of deep tendon reflexes, then by muscular weakness which may progress to paraplegia or quadriplegia. Severe constipation and even complete ileus may occur, and constipation should be avoided by a bowel program including softeners and laxatives. Cranial nerve involvement is unusual but may occur. Once neurological symptoms develop, dosage must be managed very carefully and treatment interrupted when weakness of the extremities is significant. Ordinarily time-dose related, these effects may occur quite early in the course of treatment with vincristine and must be looked for at regular visits. It is important to remind patients on vincristine of the possibility of hair loss.

The other alkylating agents (nitrogen mustard, melphalan, thiotepa, chlorambucil) have side-effects varying in degree but similar to those of Cytoxan. The other antimetabolites all depress bone marrow, like 5-FU. Velban, in contrast to vincristine, ordinarily does not produce as much peripheral neuropathy but may produce mental depression, headache, and constipation.

Any of these agents may cause marrow depression with leukopenia and thrombopenia (with the exception of bleomycin), and some of the less frequently used drugs have other side effects which will not be detailed here.

Results

The most spectacular results of chemotherapy

n cancer have been in the treatment of chorio-arcinoma, Burkitt's lymphoma, acute leukemia articularly in childhood), and certain tumors of hildhood including Wilm's tumor and neuroblas-oma. These are all relatively rare in any individ-ial practice and should be managed by physicians vith experience in their treatment since the possi-ilities for cure or for long term survival are the lirect results of intensive, knowledgeable, and vell-planned treatment.

In adults, far more common problems in the hemotherapy of disseminated malignant disease elate to cancers of the colon, breast, ovary, uterus, rostate, and the lymphomas. There is also a lace for chemotherapy, even though successful esponses are infrequent, in widespread cancer of he lung, kidney, testis, upper gastrointestinal ract and biliary system, in malignant melanoma, nd some brain tumors.

Lung Cancer

Lung cancer is the most common cause of can-er deaths in adults. When disseminated, chemo-herapeutic possibilities are limited to an objective esponse rate of perhaps five percent. Small cell ancers are somewhat more likely to respond than squamous cell cancers. When chemotherapy is used, occasional responses occur to large dose courses of Cytoxan in the small cell group. Nitro-gen mustard is somewhat more effective than Cytoxan for squamous cell cancers and can be given in conventional doses. These tumors occa-sionally will respond to a combination of actino-mycin-D and vincristine, but responses are usually of relatively short duration. Unfortunately, lung cancer commonly metastasizes to the brain where it cannot be controlled by chemotherapy, although cerebral metastases may be benefitted by radiation.

Colon Cancer

This next most common cause of cancer deaths has been treated with 5-FU with reasonable suc-cess for many years. The objective response rate is still in the range of 15-20 percent at best. There have been changes in the schedules of treatment resulting in less toxicity and greater ease of ad-ministration. Following the early intensive courses of 5-FU which often caused considerable toxicity, comparable results were produced with weekly intravenous 5-FU. Within the past two years it has been shown further that 5-FU is well tolerated and equally effective when given by mouth at weekly intervals provided, of course, that adequate doses are given. Too often 500 mg. of 5-FU are given routinely whereas larger doses should be given starting at 12 mg./kg. and raised to 15 mg./kg. per week or even slightly higher if toxicity does not occur. This can be continued indefinitely as long as the patient responds.

In the occasional patient who has poor tolerance to orally administered 5-FU, weekly intravenous administration should be resumed.

Patients with massive hepatic metastases as their major problem may be treated best by hepatic artery cannulation and infusion with 5-FU. This form of treatment also may be effective in primary hepatoma and in patients with hepatic metastases from other upper gastrointestinal cancers including metastases from pancreatic, gallbladder, and bile duct cancers.

The upper digestive tract cancers in general do less well than colon cancer, although occasional patients with stomach cancer respond to 5-FU. Cancer of the pancreas, gallbladder, and bile ducts occasionally respond to 5-FU alone but may re-spond better to intensive combined therapy using Cytoxan, 5-FU, Methotrexate and vincristine in combination.

Breast Cancer

The commonest cancer problem in females is breast cancer. When this becomes disseminated, hormonal maneuvers, basically castration premen-opausally and estrogen therapy postmenopausally, should be tried first. If these fail, and if chemo-therapy is to be given, the commonest of the chem-ical agents now used are Cytoxan and 5-FU. As many as 25 to 50 percent of such patient may have objective responses to these drugs. Cytoxan dosage varies from 50 to 200 mg. orally daily, and 5-FU should be started at 12 mg./kg. per week orally or intravenously and increased up to 15 mg./kg. to the point of mild toxicity.

In patients with very aggressive disease or when single drugs have failed, combination therapy may be tried using 5-FU, Cytoxan, Methotrexate and vincristine together. A significant number of such patients may respond even when they have failed to respond to single agents.

Ovarian Cancer

It seems established that the best results in the treatment of patients with invasive ovarian cancer are in patients whose disease can be treated with a combination of radiotherapy and chemotherapy, usually in that sequence. In those whose disease is thought to be too far advanced for radiation, chemotherapy alone using alkylating agents still

offers a good chance for palliation and prolonged survival. Thiotepa has been used extensively in the past, but Cytoxan is probably more commonly used at the present time and may be the first choice of drugs. Melphalan is effective also. The latter two may be given in intensive, short term, intermittent courses or by ongoing oral administration.

Other Cancers

In other commonly occurring cancers, such as prostatic and endometrial, hormonal agents, estrogens in the former, progestogens in the latter, continue to be the most effective. Chemical agents have relatively little effect.

In the more rarely encountered malignancies in adults, there are some good responses, particularly in testicular cancer for which Mithramycin in embryonal cell carcinoma has been quite effective. In some of the other cell types of testicular cancer, triple therapy, using as Actinomycin-D, chlorambucil, and Methotrexate is effective. Radiation after surgery remains the proper treatment of seminoma.

Hodgkin's Disease

Probably the most spectacular advance in the chemotherapy of malignancy has been in the treatment of advanced Hodgkin's disease with a combination of four drugs. This treatment is known as the MOPP program. The letters refer to nitrogen *m*ustard, *O*ncovin (vincristine), *p*rocarbazine (Matulane), and *p*rednisone. The number of responses and of complete remissions obtained is significantly greater, and the median survival of patients with stage IIIb and IV Hodgkin's disease doubled or trebled compared to results using single drugs.

There is less dramatic improvement, but nonetheless significant increased benefit from multiple drug treatment programs in patients with non-Hodgkin's lymphomas (lymphosarcoma and reticulum cell sarcoma). The MOPP schedule has been used in these diseases, or schedules in which Cytoxan is substituted for nitrogen mustard, or in which three drugs, Cytoxan, vincristine (Oncovin), and prednisone have been used in various schedules (COP).

Multiple Myeloma

The alkylating agents, melphalan and Cytoxan continue to be the drugs of choice in treating multiple myeloma. Different schedules are recommended by different investigators, with high dose, intermittent melphalan, usually given with prednisone, being recommended by some, and low dose daily maintenance melphalan by others. The long term results appear to be about the same with both.

Leukemia

The leukemias are where it all began in the modern era of chemotherapy of malignant disease. The possibilities for remission, long-term survival and even for some cures in acute leukemia, particularly in children, make it mandatory that these patients be treated only by those with wide experience in this field. The treatment of chronic leukemia with alkylating agents has changed less dramatically in the past few years. The use of hydroxyurea in chronic myelogenous leukemia represents an addition to management of that form of disease although myleran probably is still the drug of choice.

Summary

This represents an overview of the current status of the chemotherapy of malignant disease, an important modality of treatment for many cancer patients. No doubt the future will see the development of new, more sophisticated drugs. Further investigation of cellular kinetics will lead to new approaches in combination chemotherapy applying the known facts of drug action to the cyclic activity of cancer cells. Although no real successes have been reported to date, different types of adjunctive chemotherapy following surgery need to be investigated in carefully controlled studies of patients with breast and colon cancer. Finally, the use of reductive surgery, followed by chemotherapy, may lead to greater successes in the application of the new field of immunotherapy in cancer.

The value of presently available drugs and treatment schedules has been well established and offers hope to many cancer patients. They are readily available to clinicians whose practices include such patients.

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Special Article

Vietnam Psychiatry

Portrait of Anarchy

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THE MILITARY PSYCHIATRIST is frequently called in lieu of disciplinary action and asked to medevacuate as "sick" or recommend administrative separation as "unsuitable" many of those who do not function well in Vietnam. The latter is a General Discharge Under Honorable Conditions, with full award of benefits, instituted at the "Convenience of the Government."

Much of the literature deals with explaining the low frequency of psychiatric "casualties" in Vietnam,[1-3] or aspects of drug abuse among troops.[4-7] Little attention has been paid to documenting irresponsible behavior in the persons who come to psychiatric attention in a combat zone.

This paper will explore the nature of the personalities referred to a psychiatrist in Vietnam and question the logic of psychiatric intervention. It will clarify that the psychiatrist is used as an "accomplice" in the character disorder's rebellion against authority, in an attempt to suspend appropriate disciplinary action.

Method

One thousand consecutive soldiers presenting to the Psychiatric Service, First Medical Batallion, First Marine Division, Danang, Vietnam were seen by this examiner, who served as Division Psychiatrist between March, 1970 and February, 1971. Histories obtained by personal interview and questionnaire were supplemented by Service Record Books and Health Records in an attempt to accumulate data on disciplinary action, prior arrests, and illegal drug use. A clinical diagnosis was made in each case, corresponding to military nomenclature.

Results

Referrals were officially through military physicians but the real source was frequently a commanding officer, officer in charge, lawyer, sergeant or chaplain. Eight men were referred by the Brig (Military Prison) for "Clemency Evaluation." Fifteen referrals were initiated by Congressional Investigations. Two referrals were ordered by the Commandant of the Marine Corps.

Rarely had the referring physician taken a social history or made a personality diagnosis. These same physicians returned men for reevaluation with implicit demand for medevac or recommendation for administrative separation for "psy-

TABLE 1

Demographic and Clinical Data on 1000 Men Seen by a Psychiatrist in Vietnam, Mar. 1970-Feb. 1971

Branch of Service	975 Marines; 25 Navy
Enlistment	963
Tour	861 on First Tour
Length of Tour	932 Under 12 Months
Seen a Psychiatrist	
Military	126
Civilian	125
Age Range	17-46
Most Common Ages	18-23
Racial Characteristics	
Caucasian	708
Negro	231
Mexican American	30
American Indian	15
Puerto Rican American	9
Philippino American	2
South American	2
Chinese American	1
Portuguese American	1
Italian American	1
Marital Status	
Single	766
Married	234
With Children	128
Expecting	20
Separated-Divorced	47
With Children	33
Rank	
E3 or Below (Pvt, PFC, LCPL)	720
E4 (CPL)	145
E5 (SGT)	85
E6 or Above	46
Officers	4
Time On Active Duty	
1-2 Years	562
2-3 Years	164
3-4 Years	101
4 or More Years	123

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chiatric reasons."

Table 1 documents Branch of Service, Enlistment, Tour, previous Psychiatric History, Age, Race, Marital Status, Rank, and Time on Active Duty for this sample.

There were no serious suicide attempts. Twenty nine men had a past history of suicide gestures. Forty two men had verbally threatened suicide in the past.

A notable paradox was the frequency with which the military pleaded inability to deal with violent or threatening men, especially if they were presentable, intelligent or said they "could not control themselves."

Thirty one men were diagnosed Psychotic Reaction, usually associated with suspected or confirmed drug abuse. All of these were medevacuated. Many were returned to duty by the outside hospital. Nine men were diagnosed Neurotic Reaction. Nine hundred sixty men were diagnosed Personality Disorder, usually Antisocial Type, and returned to duty for disciplinary action. All of these men were seeking non-punitive escape from the military, seeking medical justification. Many hoped to gain compensation as well. Only 134 men admitted their motivation openly.

Table 2 documents frequency of disciplinary action. Approximately 590 men were presumed to be involved with illegal drugs. There was evidence that offenses and drug abuse progressed under the influence of lack of limit-setting by authority, which was taken as tacit approval. There were progressively fewer inhibitions about admitting heroin use. Sixteen men admitted regular use of heroin. Thirty five men admitted use of LSD. Alcoholism was an overwhelming problem in 130 men, but many more abused it.

Twenty two men were seen in association with the charge of murder. One man actually murdered another after his threat had been ignored. "Fraggings" (fragmentation grenade detonations) of authorities seemed to occur in commands in timidated by threats or who were ambivalently permissive and tacitly encouraging hostile behavio in their troops.

Arrest histories prior to service appear in Tabl 3. Only those guilty of assault had been jailed Sixty eight men enlisted to evade prison. Five men admitted involvement in infanticide. One hundred fourteen men admitted responsibility fo out-of-wed-lock children.

TABLE 2
Frequency of Disciplinary Action

Non-Judicial Punishment	
One	279
Two	90
Three	50
More than 3	83
Courts-Martial	
One	130
Two	17
Three	6
Brig Sentence Sustained	
One	53
Two or more	8

TABLE 3
Arrest Histories Prior to Service

Theft, Breaking & Entering	204
Fighting, Disorderly Conduct, Assault	142
Alcoholism	115
Running Away	43
Traffic Violations	61
Incorrigibility	26
Curfew Violations	15
Destruction of Property	14
Possession of Narcotics	13
Forgery	10
Murder (Not Apprehended)	5
Suspicion of Murder	5
Carrying a Concealed Weapon	7
Juvenile Offenses	7
Arson	4
Rioting	4
Pulling a Fire Alarm	2
"Accidental" Shooting of Others	2
Truancy	2
Vagrancy	2
Gas Siphoning	2
Hitchhiking	2
Fraudulent Enlistment	2
Lewd Behavior	3
Train Robbery	1
Possession of an Arsenal	1
Rape	1
Obscene Phone Calls	1
Pulling an Emergency Cord on a Train	1
Trespassing	1
Glue Sniffing	1
Non-Support	1
Fraud	1
Bigamy	1

Table 4 notes data on the parents of these men. Most were from the lower classes (based on father's occupation), however, only 26 men said their parents were on welfare.

Only 367 of these men graduated from high school. Of these, 77 got an equivalency certificate. Only eight men graduated college.

Discussion

Psychiatry is involved in attempting to protect men who refuse to honor their obligations to society as well as the military. The antisocial character glibly blames others for his conflicts, successfully evoking guilt in authority, to evade

TABLE 4
Data on Parents of 1000 Men Seen by a Psychiatrist in Vietnam, Mar. 1970-Feb. 1971

Parents Deceased	376
Divorced-Separated	309
Family on Welfare	26
Foster Parents	18
Guardians	2
Father a Professional	37
Mother an LPN or RN	26
Mother Seen By a Psychiatrist	10
Father Seen By a Psychiatrist	6
Father Arrested	13
Alcoholic	72
Suicided	1
Mother Arrested	0
Alcoholic	17
Suicided	1
Father Murdered by Mother	2
Murdered by Another	7
Mother Murdered by Father	1
Murdered by Another	2
Father Murdered another Man	1
Mother Murdered another Man	1

punishment and responsibility for his actions. The frequency with which physicians vehemently defended them was interpreted as evidence of tacit approval and permission by the physician for the character disorder to act out hostility to authority.

Dynamic understanding of motives of the character disorder shows a primary wish for revenge and punishment of the hated father, with attempts to trick him in a kind of game or challenge to accomplish casting the father in the role of the punishing person. This reflection of earlier parental relationships is designed to project responsibility to as well as demean authority, since the punishing father feels guilt at having to punish. Ambivalent object relationships were used to control others in an attempt to raise confusion and manipulate through a smokescreen of deceit. They played at appearing "borderline" to evade responsibility for their actions. There was uniformly no attempt to seek understanding of their behavior or motivation to change, only compensation for past wrongs done them.

Summary and Conclusions

This study has documented the nature of the personalities presenting to a psychiatrist in Vietnam. Conflict with authority was seen in almost every case. The psychodynamics of the conflict were discussed. Implications of this study are that psychiatric recommendations for control of lawlessness in a combat zone should include appropriate disciplinary limit-setting as a deterrent to the progressive breakdown in discipline seen with permissiveness in a combat zone. Drug abuse was seen as only one facet of conflict with authority.

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Children's Health Center Names Anesthesiology Head

Dr. Hugh D. Westgate has been named the Director of Anesthesiology at Children's Health Center and Hospital (CHC) in Minneapolis. His appointment was announced by Dr. Arnold S. Anderson, president of the health facility, now under construction at 25th Street and Chicago Avenue. The Center is expected to be completed in December. Dr. Westgate will also be in charge of the Intensive Care Unit, Pulmonary Function and Respiratory Therapy function of CHC.

Psychiatry

Emotional Reactions of Children to Hospitalization

JOHN C. DUFFY, M.D.

In recent years the child who enters the hospital can be certain of a thorough clinical investigation, whatever his presenting problem, but may find his emotional needs unmet. Even our outstanding scientific pediatric services can place a child in a situation which is excessively impersonal, concerned too little with his feelings.

The emotional reactions of children to hospitalization may be crying, whining, or screaming; clinging tenaciously to his parents; eating or sleeping poorly; struggling against treatment; resisting taking medication; becoming tense and fearful, silent, sad. and withdrawn; exhibiting regressive or compulsive behavior; and being destructive of their environment and themselves.

Some children manifest emotional reactions to hospitalization *after* they have left the hospital. i. e.: (1) eating problems, (2) sleep disturbances, (3) enuresis or encopresis, (4) regression, (5) tics, (6) depression, restlessness, anxiety, (7) terror of hospitals, (8) death fears, (9) mute states, (10) hypochondriasis and (11) hysterical symptoms.

Theoretical Explanations

The literature on this subject for the most part has explored various possible explanations for the child's emotional response to hospitalization. The author will explore the following issues: unfamiliarity, separation, sensory-motor restriction, the child's concept of the hospital, age, family, parents, and other related issues.

If unfamiliarity is the key issue, psychological preparation of the child can mitigate the ill effects. The technique available to combat unfamiliarity by providing factual and realistic information to the child, encouraging emotional expression in the child, and establishing trust and confidence between the child and the hospital staff.

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Provide Information

The task of providing information to the child is not simple. For the infant the brunt of information must be for the mother. The toddler, no longer totally protected by his mother, is still too young in development to grasp what happens to him, and can express his needs only in a primitive manner. The older child can understand what is to happen to him, why it will happen, and what he will experience. This information should be given simply, candidly, reassuringly, in detail appropriate to his general development.

Such information is necessary, for vague and undefined threats are more upsetting than a threat which is known and understood; just as unexpected stress is more upsetting than expected stress. If young children are not told the reason for hospitalization, they can get strange ideas about the reasons; for example they may feel they are being punished or being sent away forever because they have been naughty.

Timing

Timing any explanation of hospitalization for the child must be personalized probably between three weeks and three days before hospitalization. If the preparation is started too early, too much time is available for expansion and spreading of id fantasies. If preparation is done too late, the child's ego is given insufficient time to prepare its defenses. Although the mother is the ideal person to provide preparation for hospitalization, in some cases she may lack knowledge or be too anxious to be able to do the job. In that situation the task must be taken over by the nurse or doctor who finds the preparation was inadequate.

Environmental Manipulation

Environmental manipulations may make the the hospital less unfamiliar and forboding to the child, i. e. the child may bring a familiar toy or transitional object, the ward personnel wear street clothes instead of uniforms, etc. Such techniques achieve their effect by changing the general stimulus field while the preparation of the child places emphasis on changing the child.

Separation

For the pre-school child separation is traumatic because of a physical, psychological, and cognitive immaturity and dependence on his mother. The child's response to separation occurs in three phases: (1) protest, (2) despair, and (3) detachment. The initial phase, protest, may last from a few hours to a week or more. The young child is acutely distressed at having lost his mother and seeks to recapture her by the full exercise of his limited resources. He will often cry loudly, shake his cot, throw himself about and look eagerly towards any sight or sound which might prove to be his missing mother. Because his behavior suggests strong expectation that she will return, he usually rejects alternative figures who offer to do things for him, on occasion he may cling desperately to a nurse.

Despair

The phase of despair succeeds protest. The child's preoccupation with his missing mother is still evident, though his behavior suggests increasing hopelessness. He becomes quieter and may cry monotonously or intermittently. Withdrawn and inactive, he makes no demands on the environment and appears to be in a state of deep mourning. This quiet stage is sometimes, clearly erroneously, presumed to indicate a diminution of distress.

Signs of Recovery

The phase of detachment shows increased interest in surroundings, sooner or later succeeding protest and despair and is often welcomed as a sign of recovery. The child no longer rejects the nurses, accepts their care and the food and toys they bring, and may even smile and be sociable. Although this seems satisfactory, when his mother visits he may seem hardly to know her; instead of clinging to her he may remain remote and apathetic; instead of tears there is a listless turning away. He seems to have lost all interest in her.

Precautionary Treatment

Efforts at diminishing the trauma of separation have for the most part included: (1) visiting, (2) rooming-in, (3) arrangements to have the mother present during times of stress for the child. Liberal or unrestricted visiting hours normally beneficial can cause problems when an over-anxious and concerned mother is then in constant attendance to the child. Although rooming-in can make the hospital more like the family setting and is the natural thing to do, in many cultures the practical problems of space and expense limit its use. Having the parents present during examinations, painful procedures, before and after surgery, etc. is controversial.

Interpersonal Relations

The interpersonal interactions which take place in the hospital and may give rise to emotional problems can by grouped as child-staff, staff-parent, interstaff and child-child.

The child should have an opportunity for personal and direct contact with the staff. Contact limited to conflicts over rules, regulations and discipline is not adequate. Often overlooked is the effect of the child's personality on the staff who have their own emotional vulnerabilities. The key role the nurse plays in child-staff relations is not without risks for both the nurse and the child.

The nurse may identify with the child, perhaps by remembering her own childhood and her past fears in similar situations. If such feelings are acute, she may find the child's anguish too much to bear and she may react as an over-anxious mother not able to give the child the support and confidence he needs or to carry out treatment.

Doctor-Child Relationship

The child's personality can affect the physician in a different way. He may be uncertain as to how to provide the "human touch." Some things the doctor should do are: never discuss the child's condition in his presence unless in a positive fashion; be honest; keep the waiting time short before any painful treatment or other procedure; keep the parents informed; and make ward rounds friendly and informal in the child's presence.

In staff-parent relationships every effort should be made to deal with the parent's conflicts, confusion and anxiety in regards to the child's illness (not ignoring the role conflict between the nurse and mother).

Interstaff relationships which are marked by ambivalent feelings and competitiveness are destructive to the emotional health of the child.

The relationship between the children on the ward can be a very powerful force in effecting a healthy emotional climate. Children help each other face the realities of illness. Through active play, they are able to express and act out their feelings and are able to provide each other with reassurance to a far greater degree than any

adult.

Sensory-Motor Restrictions

Sensory-motor input is reduced during hospitalization. Sensory restrictions exist primarily in the lack of stimulation from people or things and motor restrictions are related to the limits imposed by bed or ward and lack of opportunities for recreation or education.

Child's Concept of Hospitalization

The greatest problem which blocks an understanding of the child's emotional needs is the adult's unfamiliarity with the child's subjective, irrational, and emotional approach to life. This must be considered in any effort to understand the child's concept of hospitalization. Most children from two to 14 years of age believe their behavior was responsible for their illness, a concept of crime and punishment, or guilt and retribution. For these children it follows logically that treatment should be painful. Other children who believed that someone else has caused their illness, for uncomprehensible reasons, nevertheless believe they are being punished. The heavy arm of morality escapes hardly a child. Children also have increased fears of death in conjunction with hospitalization, treatment, anesthesia and surgery. Not all distortions by the child are negative; some serve an important need in his defense mechanism.

Age

In general, children below five years of age are more susceptible to harmful effects of hospitalization than older children because of less social contact and experience, the reality of the mother-child interaction and separation, lack of communication ability and poor reality testing.

Family Relations and Prehospital Personality

The child's prehospital personality and the family's interpersonal relations play a significant role in the child's adjustment to hospitalization. A disturbed child prior to hospitalization may have significant adjustment problems. Parents bearing great anxiety or guilt in their attitudes associated with the child's hospitalization and illness communicate this to the child and may adversely affect the child's response.

Other Issues

There is no consistent correlation with the sex of the child. With regard to the level of objective stress, i.e. pain and discomfort or severity of the illness, the issue is not dependent on the type of seriousness of the illness or procedure, but rather on the type and depth of fantasies that are aroused. Such experiences as prior hospitalization, witnessing a frightening or painful medical procedure, and bodily exposure prime the emotional response.

Surgery

All surgical procedures are traumatic. In preparation of a child for surgery one should be knowledgeable of the special problem presented by the hyperexcitable child, the infant, the mentally retarded, and the emotionally disturbed child who faces serious problems in terms of their emotional adjustment. Such cases should have the benefit of the combined efforts of the pediatrician, surgeon and child psychiatrist.

> Dr. P. . . . had served in the Crimea, and seemed to regard a dilapidated body very much as I should have regarded a damaged garment; and, turning up his cuffs, whipped out a very unpleasant looking housewife, cutting, sawing, patching and piecing, with the enthusiasm of an accomplished surgical seamstress; explaining the process, in scientific terms, to the patient, meantime; which, of course, was immensely cheering and comfortable.*

*Louisa May Alcott, Hospital Sketches.

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(Continued to page 1173)

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(Continued to page 1175)



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[da Vinci antedated William Harvey by a little over a hundred years. It is strange to the modern mind that da Vinci with his intimate knowledge of anatomy should accept the classical solution to the problem of transfer of blood from the right heart to the left through the impermeable ventricular septum. To da Vinci the septum was less of an obstacle to the passage of blood than the pulmonary artery which after all led nowhere but into an "impermeable" network of the lungs. In any event everybody knew that the purpose of the pulmonary artery and its branches was to carry air into the heart to cool it. Ed.]

*Leonardo da Vinci on the human body by C D O'Malley and J Saunders Schuman 1952.

"Death is the only thing that ever terrifies me. I hate it."

"Why?" said the younger man, wearily.

"Because." said Lord Henry, passing beneath his nostrils the gilt trellis of an open vinaigrette box. "one can survive everything nowadays except that. Death and vulgarity are the only two facts in the nineteenth century that one cannot explain away. Let us have our coffee in the music-room, Dorian."*

*Oscar Wilde: The Picture of Dorian Gray, 1891.

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*Richard Edwards, "Where Griping Grief," 1576.

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(Continued from page 1173)

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Baldwin, Jerry J., Jr., Mr. ..... St. Paul
John, Byron L. ..... St. Cloud
Johnson, Curtis M. ..... Winona
Menefee, Edward C. ..... Albert Lea

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Lawson, Warren R. ..... Minneapolis
Loken, Merle ..... Minneapolis

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Jacott, William ..... Duluth
Kaine, Richard ..... Rochester
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FAMILY PRACTICE

Child, Sherman B. (Chairman) ..... Minneapolis
Anderson, Chester ..... Hector
Bealka, Neil ..... Stillwater
Briggs, Thomas G. ..... White Bear Lake
Cosgriff, James A., Jr. ..... Olivia
Cumming, R. J. ..... St. Cloud
Deweese, Joel T. ..... Bemidji
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Street, Bernard ..... Northfield
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HEART

(Three-year appointment)

Mankin, Harold T. (1972) (Chairman) ..... Rochester
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Anderson, John (1974) ..... Blue Earth
Boyer, S. H., Jr. (1972) ..... Duluth
Cody, Michael (1974) ..... Rochester
Dahl, James C. (1973) ..... Minneapolis
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Goott, Bernard (1973) ..... St. Paul
Hagen, John D. (1972) ..... Austin
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Hurwitz, M. M. (1973) ..... St. Paul
Johnson, Frank E. (1972) ..... Minneapolis
Johnson, Thomas (1972) ..... St. Paul
Kelly, James H. (1972) ..... St. Cloud
Kolars, Charles (1972) ..... Minneapolis
LaBree, John W. (1972) ..... Minneapolis
Luby, Thomas (1972) ..... St. Cloud
McBride, Jack (1974) ..... St. Paul
Norman, Franklin C. (1972) ..... Minneapolis
Redleaf, Paul D. (1973) ..... St. Paul
Ritter, D. G. (1972) ..... Rochester
Rusterholz, Alan P. (1972) ..... St. Paul
Ryan, Edward A. (1972) ..... Duluth
Sather, R. O. (1973) ..... Crookston
Schultz, Robert J. (1974) ..... Minneapolis
Smith, Ralph E. (1972) ..... Rochester
Spittell, John, Jr. (1973) ..... Rochester
Thiem, Chester E. (1974) ..... Mankato
Varco, Richard (1972) ..... Minneapolis

HISTORICAL

Ylvisaker, R. S. (Chairman) .....Edina
Bolz, J. Arnold .....Grand Rapids
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Dodds, William C. .....Detroit Lakes
Rosenthal, Robert .....St. Paul

INDUSTRIAL HEALTH

Ubel, Frank A. (Chairman) .....St. Paul
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Douglass, Bruce E. .....Rochester
Foker, L. W. .....Minneapolis
Fox, James Rogers .....Minneapolis
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Lawson, Warren .....Minneapolis
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Shronts, J. F. .....Minneapolis
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Henderson, E. D. .....Rochester
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Karish, Louis .....Grand Rapids
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Karleen, Conrad I. .....Minneapo
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Bernstein, Irving C. .....Minneapol
Brattensborg, Henry .....St. Clou
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Cowan, Gary .....Dulut
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Halvorson, James W. .....Zumbrot
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Janecek, James .....New Brighto
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Straus, Maurice .....St. Pa
Teeter, Richard R. .....St. Pa
Tyce, Francis A. .....Rochest
Wallinga, J. V. .....Minneapoli
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Williams, George .....St. Pa

Subcommittee on Drivers License Review (Neurology)

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Brown, Joe .....Rochest
French, Lyle .....Minneapoli
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Abuzzahab, Faruk .....Minneapoli
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Dorsey, George, Jr. .....Minneapoli
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Warner, Paul L. .....St. Clou
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Subcommittee on the Psychiatric Training Program for Non-Psychiatric Physicians

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ernstein, Irving C. ..... Minneapolis
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aberle, Charles A. ..... Minneapolis
iller, Bruce ..... Minneapolis
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rem, Konald ..... Minneapolis
osenfield, A. B. ..... Minneapolis
ozycki, Anthony ..... St. Cloud
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loffman, Walter L. ..... Minneapolis
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lorns, Richard C. ..... Minneapolis
ohnson, Douglas L. ..... Little Falls
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Kelly, James H. .....St. Cloud
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Stickney, J. M. .....Rochester

JUDICIAL

(Three-year appointment)

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Plasha, Matthew .....Coon Rapids
Van Herik, Martin .....Rochester

MEDICAL EDUCATION

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Huffington, Herb L. .....Waterville
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Kieffer, Stephen .....Minneapolis
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Lester, John .....Mapleton
Monahan, R. H. .....St. Paul
Prem, Konald .....Minneapolis
Racer, Harley .....Minneapolis
Salchert, John J. .....Minneapolis
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Tiffany, Francis B. .....St. Paul
Welch, John .....Rochester

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Plasha, Matthew K. .....Coon Rapids
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Yonehiro, Earl .....Minneapolis

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DeRemee, Richard ..... Rochester
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Hoffman, Walter L. ..... Minneapolis
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Petersen, Glenn L. ..... Minneapolis
Peterson, Willard C., Jr. ..... Minneapolis
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Lester, John ..... Mapleton
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Ciriacy, E. W. ..... Minneapolis
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MINNESOTA STATE MEDICAL ASSOCIATION
COUNTY MEDICAL SOCIETIES
Number of physicians in each county shown by figure in lower left corner.
KITTSON
ROSEAU
LAKE OF THE WOODS
MARSHALL
RED RIVER VALLEY
BELTRAMI
HEADWATERS
KOOCHICHING
ST. LOUIS
RANGE
LAKE
COOK
POLK
PENNINGTON
RED LAKE
CLEAR WATER
ITASCA
NORMAN
MAHNOMEN
HUBBARD
CASS
CLAY
BECKER
CLAY-BECKER
AITKIN
No St Louis Co
So. St. Louis Co
WADENA
CROW WING
CARLTON
ST. LOUIS
WILKIN
OTTERTAIL
UPPER MISSISSIPPI
PARK REGION DISTRICT
TODD
MORRISON
PINE
TRAVERSE
GRANT
DOUGLAS
MILLE LACS
KANABEC
EAST CENTRAL MINNESOTA
STEVENS
POPE
STEARNS
BENTON
ISANTI
CHISAGO
WEST CENTRAL MINNESOTA
BIG STONE
STEARNS-BENTON
SHERBURNE
SWIFT
KANDIYOHI
MEEKER
WRIGHT
ANOKA
WASH
HENNEPIN
CHIPPEWA
LAC QUI PARLE
MID
WRIGHT
RAMSEY
CAMP RELEASE DISTRICT
HENNEPIN
2087
720
WAKOTA
McLEOD
CARVER
23
SCOTT
DAKOTA
RENVILLE
MINNESOTA
YELLOW MEDICINE
SIBLEY
LE SEUER
RICE
GOODHUE
LINCOLN
LYON
REDWOOD
LYON-LINCOLN
NICOLLET
NICOLLET LE SUEUR
WABASHA
BROWN
WASECA
STEELE
DODGE
OLMSTED
WINONA
PIPESTONE
MURRAY
COTTONWOOD
WATONWAN
BLUE EARTH
WA-SECA
STEELE
ZUMBRO-
SOUTHWESTERN
ROCK
NOBLES
JACKSON
MARTIN
FARIBAULT
FREEBORN
MOWER
FILLMORE
HOUSTON
MINNESOTA
BLUE EARTH VALLEY
FREEBORN
MOWER
VALLEY

County Medical Society Roster

KEY TO SYMBOLS AS FOLLOWS
* Deceased
† Associate and Life
£ Resident and Intern
§ Medical Student
Service
¶ Affiliate and Honorary
‡ Wife is Member of Women's Auxiliary

BLUE EARTH COUNTY MEDICAL SOCIETY

Blue Earth County
Regular meetings, last Monday of the month
Annual meeting, December
Number of members 61

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‡ Batdorf, B. Niles .....Mankato
‡ Boade, W. A. .....Mankato
‡ Brady, Charles H. .....Mankato
† Butzer, John A. .....Mankato
Cadbury, Jane B. .....Mankato
‡ Chalgren, William S. .....Mankato
‡ Conley, Robert H. .....Mankato
Dobson, Mervin W. .....Mankato
‡ Dover, James W. .....Mankato
‡ Eckert, Joseph F. .....Mankato
‡ Eggert, Delmer C. .....Mankato
‡ Eisenbeis, Charles F. .....Mankato
‡ Elliott, J. W. .....Mankato
‡ Engstrom, Robert B. .....Mankato
‡ Eustermann, John J. .....Mankato
‡ Florine, Martin C. .....Madison Lake
‡ Fortier, R. G. .....Mankato
† Franchere, Frederick W. .....Lake Crystal
‡ Freeman, Donald H. .....Mankato
‡ Geurs, Benjamin R. .....Mankato
‡ Gislason, Paul H. .....Mankato
‡ Grande, David W. .....Mankato
‡ Hammar, Lawrence M. .....Mankato
Hankerson, Robert G. .....Mankato
Heimark, John J. .....Mankato
‡ Heller, Edgar E. .....Mankato
† Hoeper, Philip G. .....Chestnut Hill, MA
Huffington, Herb L. .....Waterville
† Huffington, Herbert L. .....Brownsville, Texas
†‡ Jones, Orville H. .....Mankato
‡ Kearney, R. Wynn .....Mankato
† Kemp, Alphonse F. .....Mankato
‡ Knowles, William D. .....Mankato
Lester, John W. .....Mapleton
‡ Lindblom, Alton E. .....Mankato
‡ Lippman, Elmer .....Mankato
† Luck, Hilda .....Mankato
‡ Lund, J. Benjamin .....Mankato
McBride, Alexander M. .....Mankato
‡ McGregor, Byron C. .....Mankato
‡ Marso, John L. .....Mankato
‡ Mathews, Wallace E. .....Mankato
‡ Meredith, Donald C. .....Mankato
Mickelson, John C. .....Los Angeles, CA
Morgan, Hugh O. .....Amboy
‡ Norris, J. C. .....Mankato
‡ O'Byrne, Alvaro .....Mankato
‡ Penn, George F. .....Mankato
‡ Roth, Frederick D. .....Mankato
‡ Rozeboom, P. T. .....Mankato
‡ Sanford, Raymond A. .....Mankato
‡ Scheidel, Alois M. .....Mankato
‡ Schmitz, Anthony A. .....Mankato
‡ Sebald, John R. .....Mankato
‡ Setzer, Hobert J., Jr. .....Mankato
‡ Sjoding, J. Donald .....Mankato
‡ Smith, Harry J. .....Lake Crystal
‡ Snider, Howard R. .....Mankato
Strobel, Claire J. .....Mankato
‡ Swenson, Donald B. .....Mankato
‡ Thiem, Chester E. .....Mankato
† Troost, H. Bradley .....Mankato
† Vezina, John C. .....Mapleton
‡ Von Drasek, Joseph .....Mankato
‡† Wentworth, Albert J. .....Mankato

BLUE EARTH VALLEY MEDICAL SOCIETY

Martin, Watonwan and Faribault Counties
Regular meetings, third Wednesday of each month
Annual meeting in November
Number of members 36

PRESIDENT
Gardner, Jack W. ..... Fairmont

SECRETARY
Boysen, Herbert ..... Madelia

‡ Anderson, John W. ..... Blue Earth
‡ Armstrong, Ralph S. ..... Winnebago
‡ Bellomo, John ..... Fairmont
†‡ Boysen, Herbert ..... Madelia
Cox, Russell L. ..... Estherville, IA
‡ Cullen, Robert M. ..... Elmore
Drexler, George W. ..... Blue Earth
‡ Feigal, William M. ..... Fairmont
‡ Gardner, Jack K. ..... Fairmont
*† Gardner, Victor H. ..... Fairmont
‡ Halverson, William G. ..... Madelia
‡ Hanson, Lewis ..... Frost
Hruza, William J. ..... Sioux Falls, SD
‡ Kraemer, George N. ..... Fairmont
‡ Krause, Carl W. ..... Fairmont
‡ Lester, Malcolm J., Jr. ..... Truman
‡ Lindahl, Merlyn J. ..... Sherburn
‡ Mijares, Wilfredo ..... Fairmont
† Mills, John L. ..... Winnebago
‡ Moulton, Keith B. ..... St. James
Nickerson, Neil D. ..... Fairmont
‡ Parsons, R. A. ..... St. James
Parsons, Ralph L. ..... Trimont
‡ Pitcher, Arlo L. ..... St. James
†‡ Russ, Homer H. ..... Blue Earth
‡ Schotzko, John R. ..... Blue Earth
Schulz, Robert W. ..... Fairmont
Smith, Don V. ..... Blue Earth
‡ Tempel, J. W. ..... Blue Earth
‡ Thayer, Ellsworth A. ..... Fairmont
‡ Virnig, Mark P. ..... Wells
‡ Virnig, Richard P. ..... Wells
‡ Wandke, Otto E. ..... Fairmont
‡ Watkins, John A. ..... Wells
‡ Williamson, Harold A. ..... Fairmont
‡ Zemke, Erhart E. ..... Fairmont
‡ Zemke, Robert L. ..... Fairmont

BROWN COUNTY MEDICAL SOCIETY

Brown County
Regular meetings, second Tuesday
January, April, July and October
Annual meeting in January
Number of members 27

PRESIDENT
Kaiser, Milton ..... New Ulm

SECRETARY
Vogel, Ann ..... New Ulm

‡ Black, William A. ..... New Ulm
‡ Boyle, Francis J. ..... Springfield
‡ Burnett, Joseph W. ..... New Ulm
‡ Cairns, Robert J. ..... Redwood Falls
‡ Carthey, Frank J. ..... New Ulm
Fesenmaier, Otto B. ..... Pasadena, CA
† Fritsche, Albert ..... New Ulm
‡ Fritsche, Carl J. ..... New Ulm
‡ Fritsche, Theodore R. ..... New Ulm
Gilles, Thomas F. ..... Fairfax
† Goblirsch, Andrew P. ..... Wayzata
‡ Johnson, Rex R. ..... New Ulm
‡ Kaiser, Milton L. ..... New Ulm
‡ Keithahn, Elmer E. ..... Sleepy Eye
‡ Kitzberger, Peter J. ..... New Ulm
Muesing, William J. ..... New Ulm
† Nuessle, Walter G. ..... Springfield
‡ Penk, Engward L. ..... Springfield
† Peterson, Roy A. ..... Vesta
‡ Rimas, Mathew J. ..... Comfrey
Ringhofer, Lawrence ..... New Ulm
‡ Saffert, Cornelius A. ..... New Ulm
Vogel, Ann C. ..... New Ulm
Vogel, Howard A. ..... New Ulm
Wing, Elton G. ..... Sleepy Eye
Wohlrabe, Donald E. ..... Springfield
†‡ Wohlrabe, Edwin J. ..... Springfield

CAMP RELEASE DISTRICT MEDICAL SOCIETY

Chippewa, Lac qui Parle and Yellow Medicine Counties
Regular meetings, second Thursday of each month
except July and August
Annual meeting, December
Number of members 23

PRESIDENT
Camp, Ray J. ..... Madison

SECRETARY
Westby, Norval M. ..... Madison

‡ Allen, John H. ..... Montevideo
‡ Anderson, Chester A. ..... Madison
‡ Birkey, Thomas G. ..... Montevideo
‡ Boody, George J. ..... Cambridge
‡ Borgerson, M. A. ..... Hanley Falls
† Burns, Floyd M. ..... Milan
‡ Camp, Ray J. ..... Madison
‡ Carter, Kenneth R. ..... Granite Falls
‡ Hagberg, Norman L. ..... Montevideo
†‡ Hauge, Malvin I. ..... Marcell
‡ Johnson, Vilhelm M. ..... Dawson
¶ Jordan, Kathleen B. Smith ..... Granite Falls
*† Kaufman, William C. ..... Appleton

Camp Release District Medical Society *(Continued)*
‡ Kremer, Jerome L. .....Montevideo
‡ Lima, Ludvig R. .....Montevideo
‡ Lundell, Carl L. .....Granite Falls
‡ Maus, Philip W. .....Dawson
‡ Niazi, Suad A. .....Granite Falls
‡ Owens, William A. .....Montevideo
‡ Radke, Robert L. .....Milan
‡ Rifat, Baseem M. .....Clarkfield
Roust, Henry A. .....Montevideo
‡ Schmidt, Paul G. .....Granite Falls
‡ Westby, Norval M. .....Madison

CLAY-BECKER COUNTY MEDICAL SOCIETY

Clay and Becker Counties
Regular meeting date, April
Annual meeting, November
Number of members 31

PRESIDENT
Norberg, William J. .....Detroit Lakes
SECRETARY
Ekberg, Fred .....Detroit Lakes
Bigler, Earl E. .....Perham
Bigler, Ivan E. .....Perham
‡ Bologna, Camillo V. .....Moorhead
† Bottolfson, B. T. .....Moorhead
Brenk, Paul E. .....Detroit Lakes
Broadhurst, Kennon E. .....Detroit Lakes
Carlon, Donald L. .....Moorhead
‡ Carlson, Vernon J. .....Moorhead
‡ Colliton, Patrick A. .....Moorhead
‡ Covey, Kenneth W. .....Moorhead
Dodds, William C. .....Detroit Lakes
‡ Duncan, James W. .....Moorhead
Ekberg, Fred .....Detroit Lakes
‡ Geib, Marvin J. .....Fargo, ND
Good, Richard .....Detroit Lakes
‡ Holten, John .....Moorhead
† Johnson, Olga H. .....Moorhead
Knapp, James F. .....Detroit Lakes
Koons, William R. .....Mahnomen
Lorentzen, Ernest S. .....Detroit Lakes
Midthune, Andreen S. .....Lake Park
Nakamura, James Y. .....Detroit Lakes
Norberg, William J. .....Lake Park
Odland, Mark E. .....Detroit Lakes
‡ Rice, Hagbart G. .....Moorhead
Rutledge, John B. .....Detroit Lakes
† Rutledge, Lloyd H. .....Detroit Lakes
Saxman, Gertrude O. .....Ulen
‡ Simison, Carl .....Barnesville
‡ Thysell, Vernon D. .....Moorhead
Watson, Robert N. .....Detroit Lakes
Watson, Virgil A. .....Detroit Lakes

EAST CENTRAL MINNESOTA MEDICAL SOCIETY

Anoka, Chisago, Isanti, Kanabec, Mille Lacs,
Pine and Sherburne Counties
Regular meetings first Tuesday of even
months of the year except August
Annual meeting, first Tuesday in December
Number of members 39

PRESIDENT
Brettingen, Larry .....Mora
SECRETARY
Seecamp, Carsten .....Cambridge
† Aruguete, Alayne .....St. Paul
*‡ Berge, Harry L. .....Mora
‡ Berglund, Alvin E. .....Cambridge
‡ Brettingen, Larry J. .....Mora
Bunker, Bevan W. .....Anoka
‡ Burseth, Edgar C. .....Mora
‡ Deason, Keith B. .....Chisago City
Doebler, Myron I. .....Princeton
‡ Erickson, Carlton .....Lindstrom
‡ Ericsson, Kermit C. .....Cambridge
Gailitis, Veronika M. .....St. Paul
† Grinvalds, Anna O. .....St. Paul
‡ Hartzler, Paul L. .....Cambridge
‡ Hovde, Gordon W. .....Chisago City
Huber, Robert W. .....St. Croix Falls, WI
Hubin, Edwin G. .....Sandstone
Johnson. Aldridge F. .....Isanti
† Kelsey, Carleton G. .....St. Paul
‡ Lamusga, David J. .....Cambridge
‡ Larson, Gerald E. .....Cambridge
‡ Lindquist, Dale C. .....Lindstrom
‡ Mach, Ralph F. .....Pine City
‡ Magnuson, Raymond C. .....Cambridge
Metcalf, Norman .....Princeton
‡ Nelson, Luther A. .....Rush City
‡ Nordman, Willard F. .....Mora
Nygren, William T. .....Braham
‡ Overgaard, Peter H. .....Lindstrom
‡ Peterson, Alvin C. .....Mora
‡ Pivac (Popovich) Dragojla .....Milwaukee, WI
‡ Reiners, Gary .....Cambridge
‡ Ristic, Miodrag .....Cambridge
†‡ Roehlke, Arthur E. .....Elk River
‡ Runquist, Richard .....Cambridge
*† Schut, John W. .....Anoka
‡ Seecamp, Carsten H. .....Cambridge
Sommer, R. K. .....Elk River
† Spurzem, Raymond J. .....Anoka
†‡ Stratte, Alf K. .....Pine City
‡ Tesch, Gordon H. .....Elk River
‡ Travis, Richard C. .....Elk River

FREEBORN COUNTY MEDICAL SOCIETY

Freeborn County
Regular meetings, third Thursday of even months
Annual meeting, December
Number of members 35

PRESIDENT
Cole, George A. ..... Albert Lea
SECRETARY
Ellertson, Leonard M. ..... Albert Lea
‡ Barr, Lowell C. ..... Albert Lea
‡ Barr, Lowell W. ..... Albert Lea
‡ Bartness, John E. ..... Albert Lea
‡ Blumer, Arlo R. ..... Albert Lea
‡ Buege, William ..... Albert Lea
† Burns, Catherine ..... Excelsior
Burns, James F. ..... Albert Lea
Cole, George A. ..... Albert Lea
‡ Demo, Robert A. ..... Albert Lea
Donovan, Daniel L. ..... New Brighton
‡ Egge, Sanford G. ..... Albert Lea
‡ Ellertson, Leonard M. ..... Albert Lea
‡ Erdal, Ove A. ..... Albert Lea
Gamble, Elbert J. ..... Roseville
‡ Gill, Theodore M. ..... Albert Lea
‡ Halvorson, Harold C. ..... Albert Lea
‡ Hansen, Theodore M. ..... Albert Lea
‡ Keil, Marcus A. ..... Albert Lea
† Leopard, Brand A. ..... Brownsville, TX
‡ Menefee, Edward C. ..... Albert Lea
Myers, Theodore P. ..... Albert Lea
‡ Neel, Harry B. ..... Albert Lea
‡ Nelson, Clayton E. J. ..... Albert Lea
Nesheim, Martin O. ..... Albert Lea
†‡ Palmer, Clinton F. ..... Albert Lea
Rose, Cordt ..... Albert Lea
‡ Schmidt, Ruben F. ..... Alden
‡ Shepard, Richard ..... Albert Lea
‡ Sherman, Alfred G. ..... Albert Lea
‡ Steiner, Leon E. ..... Albert Lea
Stoker, Lynn C. ..... Albert Lea
‡ Thompson, Thoburn F. ..... Albert Lea
‡ Treanor, Thomas A. ..... Albert Lea
‡ Whitson, Sidney A. ..... Albert Lea
‡ Wilcox, G. Charles ..... Albert Lea
‡ Willie, James A. ..... Albert Lea

GOODHUE COUNTY MEDICAL SOCIETY

Goodhue County
Regular meeting, April and November
Annual meeting, November
Number of members 28

PRESIDENT
Delahunty, John R. ..... Red Wing
SECRETARY
Friedrich, Bradford ..... Red Wing
‡ Akins, Willard M. ..... Red Wing
‡ Billings, Harry H. ..... Red Wing
‡ Biltz, John F. ..... Red Wing
†‡ Brusegard, James F. ..... Red Wing
‡ Cant, Wilbur F. ..... Red Wing
‡ Delahunty, John R. ..... Red Wing
Douglass, Jesse E. ..... Cannon Falls
Falls, John L. ..... Red Wing
‡ Fauchald, Nils, Jr. ..... Red Wing
Friedrich, Bradford E. ..... Red Wing
‡ Halvorson, James W. ..... Zumbrota
‡ Hartnagel, Grant F. ..... Red Wing
‡ Hawley, George M. B. ..... Red Wing
‡ Jackish, George E. ..... Red Wing
‡ Juers, Edward H. ..... Red Wing
Kuehner, Marvin E. ..... Red Wing
‡ Larson, Oliver E. H. ..... Zumbrota
Marshall, John F. ..... Pine Island
‡ Molenaar, Robert E. ..... Cannon Falls
‡ Moshfeghi, Mohammad M. ..... Red Wing
Rayner, Ralph R. ..... Red Wing
‡ Roth, Charles W. ..... Red Wing
‡ Sander, John L. ..... Red Wing
Schroeder, Glenn E. ..... Red Wing
‡ Sherman, Royal V. ..... Red Wing
Walter, William E. ..... Wanamingo
‡ Wasmund, Clarence W. ..... Red Wing
‡ Williams, Marland R. ..... Cannon Falls

HEADWATERS MEDICAL SOCIETY

Beltrami, Clearwater and Lake of the Woods Counties
Regular meetings to be determined
Annual meeting, 2nd Saturday in September
Number of members 24

PRESIDENT
Hoganson, Donald ..... Bemidji
SECRETARY
Gregoire, Earl ..... Bemidji
Brink, Adlai A. ..... Baudette
Deweese, Joel T. ..... Bemidji
Deweese, Wilford J. ..... Bemidji
Franklin, Gordon W. ..... Northome
Gregoire, Earl ..... Bemidji
Griffin, John W. ..... Bemidji
Hildebrand, John E. ..... Bemidji
Hoganson, Donald E. ..... Bemidji
Janecky, Allen G. ..... Baudette
† Johnson, Einer W. ..... Bemidji
† Larson, Leroy J. ..... Bagley
Lundsten, Leslie C. ..... Bemidji
Martin, Frederick F. ..... Bagley
Nordlund, Mildred E. ..... Cass Lake
Palmer, Harry A. ..... Blackduck
Pearson, Harris L. ..... Bagley
Reeber, Erick ..... Bagley
Reid, Howard ..... Bemidji
Roholt, Hartvig B. ..... Bemidji
Thompson, James R. ..... Bemidji
Whittemore, Dexter D. ..... Bemidji
Will, Theodore J. ..... Bemidji
Wilson, Bruce C. ..... Bemidji
Wohlfiel, Dwayne L. ..... Bemidji

HENNEPIN COUNTY MEDICAL SOCIETY

Hennepin County
Regular meetings, first Monday of the Months of
October, January, March and May, except when
otherwise designated
Annual meeting, first Monday in October
Number of members 1429

PRESIDENT
Mankey, James C. ..... Minneapolis
SECRETARY
Lund, George W. ..... Minneapolis
EXECUTIVE SECRETARY
Hoban, Thomas W., Mr. ..... Minneapolis

Abramson, Burton I. ..... Minneapolis
Abramson, Milton ..... Minneapolis
‡ Abullarade, Jose A. ..... Minneapolis
‡ Abuzzahab, Faruk S., Sr. ..... Minneapolis
‡ Adams, Brandon, L. W. ..... Minneapolis
‡ Adams, Richard I. ..... Minneaplois
‡ Adicoff, Arnold ..... Minneapolis
Adkins, C. Douglas ..... Minneapolis
‡ Adkins, James T. ..... Coon Rapids
‡ Agustsson, Hreidar ..... Minneapolis
‡ Ahern, Eugene E. ..... Minneapolis
Akbar, Sajady ..... Minneapolis
‡ Aksoy, Mustafa M. ..... St. Paul
‡ Alari, Heino ..... Excelsior
*‡ Alexander, Harlan A. ..... Minneapolis
†‡ Aling, Charles A. ..... Minneapolis
Alkon, Ellen ..... Minneapolis
‡ Allen, James R. ..... Minneapolis
Alter, Milton ..... Minneapolis
‡ Amatuzio, Donald S. ..... Minneapolis
‡ Amren, Don P. ..... Minneapolis
‡ Anderegg, Alfred F. ..... Minneapolis
Andersen, James G. ..... Minneapolis
‡ Andersen, Robert C. ..... Minneapolis
‡ Anderson, Arnold S. ..... Minneapolis
Anderson, David M. ..... Minneapolis
†‡ Anderson, Ernest R. ..... Minneapolis
‡ Anderson, Frank J. ..... Minneapolis
Anderson, John A. ..... Minneapolis
†‡ Anderson, Karl W. ..... Excelsior
‡ Anderson, Quentin N. ..... Minneapolis
Anderson, Richard W. ..... Minneapolis
Anderson, Roger E. ..... Minneapolis
‡ Anderson, Roger L. ..... Minneapolis
Anderson, Thomas P. ..... Minneapolis
‡ Anderson, U. Schuyler ..... Fort Snelling
Anderson, Wallace E. ..... Minneapolis
‡ Anderson, William H. ..... Minneapolis
Anderson, William T. ..... Minneapolis
Anderson, W. Robert ..... Minneapolis
Andre, James C. ..... Minneapolis
† Andreassen, Einar C. ..... Minneapolis
‡ Andreassen, Rolf L. ..... Minneapolis
‡ Andresen, Karl d'A ..... Minneapolis
‡ Ankner, Frank J. ..... Minneapolis
Anonsen, Richard E. ..... Minneapolis
Anselment, Lois A. ..... Excelsior
*† Arends, Archabald L. ..... Minneapolis
Arenson, Jeffrey A. ..... Minneapolis
‡ Arey, Stuart Lane ..... Minneapolis
‡ Arhelger, Stuart W. ..... Minneapolis
‡ Arlander, Clarence E. ..... Minneapolis
Arlander, Thomas R. ..... Minneapolis
‡ Arling, Leonard S. ..... Minneapolis
Arms, James J. ..... Minneapolis
Armstrong, Byron H. ..... Minneapolis
† Arnold, Ann W. ..... Minneapolis
Arnold, Thomas B. ..... Minneapolis
Aughenbaugh, John W. ..... Minneapolis
‡ Avant, Robert F. ..... Minneapolis
Azad, Manouchehr ..... Minneapolis
Bachmann, Sigrid A. ..... St. Paul
‡ Backus, Reno E. ..... Minneapolis
‡ Baggenstoss, Osmond J. ..... Minneapolis
‡ Bagley, Russell W. ..... Minneapolis
*†‡Baken, Melvin P. ..... St. Paul
Baken, Melvin P., Jr. ..... Minneapolis
Baker, Abe B. ..... Minneapolis
‡ Baker, C. Camak ..... Minneapolis
‡ Baker, Daniel R. ..... Minneapolis
‡ Baker, Lowell ..... Minneapolis
‡ Baker, Milton E. ..... Minneapolis
Bakke, Arnold C. ..... Minneapolis
‡ Balcos, Emmanuel G. ..... Minneapolis
‡ Balkin, Samuel G. ..... Minneapolis
‡ Balkins, John W. ..... Minneapolis
‡ Balogh, Charles J. ..... Minneapolis
Bandt, Calvin M. ..... Minneapolis
† Bank, Harry E. ..... Minneapolis
Banovetz, John D. ..... Minneapolis
‡ Barnett, Robert M. ..... Minneapolis
‡ Barno, Alex ..... Minneapolis
‡ Barr, Maxwell M. ..... Minneapolis
‡ Barrett, Patrick J. ..... Minneapolis
‡ Barron, Jesse J. ..... Minneapolis
†‡ Barron, Moses ..... Beverly Hills, CA
‡ Barry, George J. ..... Minneapolis
Bart, Bruce J. ..... Minneapolis
Baumgartner, C. John ..... Minneapolis
‡ Beach, Northrop ..... Minneapolis
Beard, Archibald H., Jr. ..... Minneapolis
Becklund, Roger W. ..... Minneapolis
‡ Beeman, John A. ..... Minneapolis
Beirstein, Samuel ..... Minneapolis
† Beiswanger, Richard H. ..... Edina
‡ Bell, Donald C. ..... Minneapolis
Bellville, Titus P. ..... Minneapolis
Belzer, Meyer S. ..... Minneapolis
‡ Bendel, Richard P. ..... Minneapolis
Bendel, William L., Jr. ..... Coon Rapids
Benesh, Louis A. ..... Minneapolis
‡ Benjamin, Edwin G. ..... Minneapolis
‡ Benjamin, Harold G. ..... Minneapolis
Benjamin, Richard D. ..... Minneapolis
‡ Benjamin, Robert B. ..... Minneapolis
Bensman, Alan S. ..... Minneapolis
‡ Bentz, Herman D. ..... Anoka
‡ Berestka, Stephen J. ..... Minneapolis
Berg, Clinton C. ..... Excelsior
Berger, Alex G. ..... Minneapolis
‡ Bergh, George S. ..... Minneapolis

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Hennepin County Medical Society *(Continued)*

Bergh, Solveig M. ....Minneapolis
‡ Berglund, Eldon B. ....Minneapolis
‡ Bergquist, James R. ....Minneapolis
Bergstrom, Ralph W., Jr. ....Maple Plain
‡ Bergstrom, William J. ....Minneapolis
† Berkwitz, Nathaniel J. ....Minneapolis
Berman, David A. ....Minneapolis
Berman, Reuben ....Minneapolis
Bernstein, Dorothy M. ....Minneapolis
Bernstein, Irving C. ....Minneapolis
‡ Berris, Harold ....Minneapolis
Berry, Ronald N. ....Minneapolis
‡ Berzins, Rainis ....Minneapolis
†‡ Bessesen, Alfred N. ....Minneapolis
‡ Bevis, William D. ....Minneapolis
Bieger, R. Cyril ....Minneapolis
Biery, M. Barbara ....Minneapolis
Bieter, Raymond N. ....Minneapolis
‡ Bilgutay, Aydin M. ....Minneapolis
Bilka, Paul J. ....Minneapolis
Billman, Herbert R. ....Minneapolis
Binder, Manuel R. ....Minneapolis
Bittick, Wilbur H. ....Minneapolis
‡ Blackard, Clyde E. ....Minneapolis
‡ Blake, Allan J. ....Hopkins
‡ Blake, James A. ....Hopkins
‡ Blake, Paul S. ....Minneapolis
* Bloch, Henry S. ....Minneapolis
‡ Bloedel, Traugott J. ....Osseo
‡ Blomberg, Robert D. ....Minneapolis
‡ Bloom, David ....Minneapolis
Bloom, Norman B. ....Minneapolis
‡ Blumenthal, Malcolm N. ....Minneapolis
‡ Boardman, Peter J. ....Wayzata
‡ Boardman, William J. ....Minneapolis
Bofenkamp, Benjamin ....Minneapolis
*†‡ Bohn, Donald G. ....Minneapolis
†‡ Boies, Lawrence R., Sr. ....Hopkins
Boller, M. A. ....Minneapolis
£ Bolt, Donald A. ....Minneapolis
‡ Bonewell, George W. ....Minneapolis
‡ Borman, Chauncey N. ....Minneapolis
Borowicz, Leonard A. ....Minneapolis
Borrud, Chester C. ....Anoka
Bouthilet, Florence J. ....Minneapolis
† Bowers, Gordon G. ....Excelsior
‡ Bowlin, Paul F. ....Minneapolis
† Boynton, Ruth E. ....Miami, FL
£ Boyum, Allan J. ....Minneapolis
‡ Bradford, David S. ....Minneapolis
Bradley. Jeanne B. ....Minneapolis
Bradley, John G. ....Minneapolis
Bradley, William E. ....Minneapolis
‡ Brandt, Henry E. ....Minneapolis
‡ Bransford, Paul W. ....Minneapolis
‡ Brauer, William W. ....Minneapolis
‡ Braun, Rene ....Minneapolis
‡ Breitenbucher, Robert B. ....Minneapolis
†‡ Brekke, Harvey J. ....Minneapolis
‡ Brennan, Joseph G. ....Minneapolis
Brill, Alice K. ....Minneapolis
‡ Briones, Bienvenido R. ....Hopkins
‡ Bromer, Michael D. ....Minneapolis
† Brooks, Charles N. ....Wayzata
‡ Brown, John H. ....Minneapolis
‡ Brown, William D., Jr. ....Minneapolis
‡ Brownfield, James A. ....Minneapolis
‡ Buchstein, Harold F. ....Minneapolis
‡ Buckley, Joseph J. ....Minneapolis
‡ Bugby, Robert D. ....Minneapolis
‡ Bugenstein, Robert H. ....Minneapolis
‡ Buie, Louis A., Jr. ....Minneapolis
‡ Bundt, Robert E. ....Minneapolis
‡ Buran, David J. ....Minneapolis
‡ Burchell, Howard G. ....Minneapolis
Burke-Strickland, Martha ....Minneapolis
Burkholder, Dayton D. ....Anoka
‡ Burnham, Wesley H. ....Minneapolis
Burton, Thomas P. ....Minneapolis
‡ Cable, Morris L. ....Minneapolis
† Cabot, Clyde M. ....Deerfield Beach, FL
‡ Calin, S. Hartley ....Minneapolis
Cameron, Bruce P. ....Minneapolis
† Cameron, Isabell L. ....Minneapolis
‡ Campbell, Denis V. ....Minneapolis
Campbell, Marilyn R. M. ....Minneapolis
† Campbell, Orwood J. ....Minneapolis
† Campbell, Ronald G. ....Minneapolis
‡ Card, William H. ....Minneapolis
Cardle, James G. ....Minneapolis
‡ Cardle, John B. ....Minneapolis
‡ Carlander, Lester W. ....Minneapolis
‡ Carlson, Charles V. ....Mound
‡ Carlson, Curtis H. ....Minneapolis
Carlson, David J. ....Minneapolis
‡ Carlson, Lawrence ....Minneapolis
Carr, William J. ....Minneapolis
‡ Carrier, Thomas C. ....Minneapolis
Carrasco, Enrique ....Minneapolis
‡ Caspers, Carl G. ....Minneapolis
‡ Cauble, Charles F. ....Minneapolis
†‡ Cavanor, Frank T. ....Minneapolis
‡ Cavert, H. Mead ....Minneapolis
‡ Ceder, Elmer T. ....Minneapolis
‡ Cella, Joseph A. ....Minneapolis
‡ Chadbourn, Wayne A. ....Minneapolis
Challman, S. Alan ....Minneapolis
‡ Chandler, William M. ....Minneapolis
‡ Chedister, Charles R. ....Minneapolis
Chervenak, William A. ....Marine-on-St. Croix
‡ Chesler, Merrill D. ....Minneapolis
Child, Sherman B. ....Minneapolis
† Chilgren, Keith V. ....Minneapolis
‡ Chisholm, Tague C. ....Minneapolis
Chou, Shelley N. ....Minneapolis
‡ Christensen, Llewellyn E. ....Minneapolis
Christenson, Leland R. ....Maple Plain
Christgau, Roger A. ....Minneapolis
Christian, William L. ....Minneapolis
Cich, John A. ....Minneapolis
‡ Clark, Malcolm D. ....Minneapolis
Clark, Robert S. ....Minneapolis
Clay, Lyman B. ....Minneapolis
‡ Cline, David W. ....Minneapolis
‡ Cochrane, Ray F. ....Minneapolis
Coe, John I. ....Minneapolis
Cohan, Richard C. ....Minneapolis
‡ Cohen, Bernard A. ....Minneapolis
Cohen, Ephraim B. ....Minneapolis
‡ Cohen, Henry W. ....Wayzata
Cohen, Summer S. ....Minneapolis
‡ Cole, James S. ....Minneapolis
Coleman, Thomas P. ....Minneapolis
‡ Conlin, F. Dixon ....Minneapolis
‡ Conlon, Daniel C. ....Minneapolis

Hennepin County Medical Society *(Continued)*

† Connor, David G. ..... Minneapolis
‡ Cooper, John P. ..... Minneapolis
‡ Cooper, Robert R. ..... Minneapolis
† Corniea, Albert D. ..... Minneapolis
Correa, Dale H. ..... Minneapolis
Corson, Wilfred A. ..... Minneapolis
‡ Cortez, Daniel P. ..... Minneapolis
‡ Coulter, Harold E. ..... Minneapolis
Cowan, Donald W. ..... Minneapolis
Craig, M. Elizabeth ..... Minneapolis
†‡ Cranmer, Richard R. ..... Laguna Hills, CA
Cranston, Robert W. ..... Minneapolis
‡ Creevy, Charles D. ..... Minneapolis
† Crossley, Kent B. ..... Newtonville, MA
‡ Crowley, Leonard V. ..... Minneapolis
Cruz, Waldemar F. ..... Minneapolis
‡ Cullado, Andrionico F. ..... Minneapolis
Culligan, Leo C. ..... Minneapolis
‡ Cundy, Donald T. ..... Minneapolis
‡ Curran, John P. ..... Minneapolis
Cushing, Richard T. ..... Minneapolis
† Cutts, George ..... Minneapolis
‡ Daggett, Donald R. ..... Minneapolis
Dahl, James C. ..... Minneapolis
† Dahl, John A. ..... Minneapolis
Dahlstrom, Donald D. ..... Minneapolis
† Daniel, Donald H. ..... Minneapolis
Daniels, Clarke G. ..... Minneapolis
‡ Danoff, David ..... Minneapolis
‡ Danyluk, Michael ..... Minneapolis
Dargay, Cyril P. ..... Minneapolis
‡ Daumann, Roy E. ..... Minneapolis
David, Reuben ..... Hopkins
Davis, Curtis E. ..... Minneapolis
‡ Davis, Michael W. ..... Minneapolis
Davis, Thomas H. ..... Minneapolis
Dawson W. John, Jr. ..... Minneapolis
‡ Dedeker, Kenneth L. ..... Minneapolis
Delzell, Allen W. ..... Minneapolis
‡ Diamond, Robert A. ..... Minneapolis
Dickman, Roy W. ..... Minneapolis
Diefenbach, Eugene J. ..... Minneapolis
Diego, Benito B. ..... Fridley
† Diehl, Harold S. ..... New York, NY
Diehl, James J. ..... Minneapolis
‡ Dierker, Heinrich A. ..... Minneapolis
† Diessner, Henry D. ..... Hopkins
Dimants, Janis, Jr. ..... Minneapolis
‡ Doan, Robert E. ..... Wayzata
† Dobrin, Dale T. ..... Minneapolis
Docherty, John A. ..... Minneapolis
‡ Donatelle, Edward P. ..... Minneapolis
† Dorge, Richard ..... Minneapolis
Dornbach, Robert A. ..... Minneapolis
‡ Dorsey, George C., Jr. ..... Minneapolis
‡ Dorsey, William E. ..... Minneapolis
Doscherholmen, Alfred ..... Minneapolis
‡ Dougan, Jerome W. ..... Minneapolis
doVale, Joao M. ..... Edina
† Doxey, Gilbert L. ..... Minneapolis
‡ Dredge, Thomas E., Sr. ..... Minneapolis
‡ Dredge, Thomas E., Jr. ..... Minneapolis
‡ Drill, Frederick E. ..... Minneapolis
‡ Drill, Herman E. ..... Hopkins
Dummer, Donald J. ..... New Brighton
Dumonceau, Roland G. ..... Minneapolis
Duncan, Donald A. ..... Minneapolis
Dunkel, Thomas B. ..... Minneapolis
‡ Dunlap, David J. ..... Minneapolis
‡ Dunlap, Earl H. ..... Minneapolis
‡ Dupont, Joseph A. ..... Excelsior
Duryea, Willis M. ..... Minneapolis
‡ Duryea, Willis M., Jr. ..... Minneapolis
‡ Dvorak, Benjamin A. ..... Minneapolis
‡ Dwan, Paul F. ..... Minneapolis
† Dworsky, Samuel D. ..... Minneapolis
Earl, Stephan H. ..... Minneapolis
Ebert, Richard V. ..... Minneapolis
Eckerly, Jean R. ..... Minneapolis
‡ Eder, Walter P. ..... Minneapolis
Edmondson, Hugh A., Jr. ..... Minneapolis
‡ Efteland, Myles E. ..... Minneapolis
*† Ehrenberg, Claude J. ..... Boca Raton, FL
‡ Ehrlich, S. Paul ..... Minneapolis
Eich, Matthew A. ..... Minneapolis
Eichenlaub, John E. ..... Minneapolis
‡ Eichhorn, Edmund P., Jr. ..... Minneapolis
£ Eichten, John G. ..... Minneapolis
Eifrig, David E. ..... Minneapolis
‡ Einzig, Mitchell J. ..... Wayzata
Eisenberg, M. Michael ..... Minneapolis
‡ Eisenstadt, William S. ..... Minneapolis
Eitel, George D. ..... Minneapolis
Ellingson, Richard B. ..... Minneapolis
Ellington, Anna L. ..... Minneapolis
‡ Ellis, Cassius M. C. ..... Minncapolis
‡ Ellis, John C., Jr. ..... Minneapolis
‡ Ellison, Evan S. ..... Minneapolis
Elwood, Paul M., Jr. ..... Minneapolis
† Emond, Joseph S. ..... Farmington
Emond, Joseph S., Jr. ..... Farmington
‡ Engel, Joseph P. ..... Minneapolis
‡ Engel, William L. ..... Minneapolis
‡ Englund, Elvin F. ..... Minneapolis
† Engstrand, Oscar J. ..... Minneapolis
‡ Engstrom, E. Duane ..... Minneapolis
‡ Engwall, Richard L. ..... Minnetonka
*‡ Erickson, Clifford O. ..... Minneapolis
‡ Erickson, Laurence F. ..... Minneapolis
‡ Erickson, Myron E. ..... Minneapolis
*†‡ Erickson, Reuben F. ..... Minneapolis
£ Ersek, Robert A. ..... Minneapolis
‡ Eselius, Erik P. ..... Minneapolis
‡ Esensten, Sidney ..... Minneapolis
‡ Ettinger, Milton G. ..... Minneapolis
Etzwiler, Donnell D. ..... Minneapolis
†‡ Evans, Edward T. ..... Minneapolis
‡ Everhart, Clarence E., Jr. ..... Minneapolis
Everly, Stephan S. ..... Minneapolis
Fallon, Virgil T. ..... Minneapolis
Farber Abigail F. ..... Minneapolis
Farber, Roger E. ..... Minneapolis
‡ Farber, Lawrence A. ..... Minneapolis
Farley, Harrison H. ..... Minneapolis
Farrell, T. Edwin ..... Minneapolis
Fehr, Peter E. ..... Minneapolis
‡ Feigal, David W. ..... Wayzata
Feinberg, Philip ..... Minneapolis
Feinberg, Samuel B. ..... Minneapolis
‡ Fernandez, Rafael F., Jr. ..... Minneapolis
‡ Fetzek, Albert D. ..... Minneapolis
‡ Field, Charles W. ..... Minneapolis
Fifer, Ellen Z. ..... St. Paul
Fifer, William R. ..... Minneapolis
Filiatrault, L. J. ..... Coon Rapids
Filipovich, Orest N. ..... Minneapolis
‡ Fingerman, David L. ..... Minneapolis

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Hennepin County Medical Society *(Continued)*

†‡ Fink, Leo W. ..... Minneapolis
‡ Fink, Robert J. ..... Minneapolis
‡ Finkelstein, Joel ..... Minneapolis
Finlayson, Richard E. ..... Minneapolis
‡ Finstad, James E. ..... Minneapolis
£‡ Fischer, Albert P. ..... Minneapolis
† Fisher, Albert P., Jr. ..... Minneapolis
Fisher, Don H. ..... Minneapolis
Fisher, Howard W. ..... Minneapolis
Fisher, Isadore ..... Minneapolis
Fleming, Dean S. ..... Minneapolis
‡ Fliehr, Richard R. ..... Minneapolis
‡ Flora, George C. ..... Minneapolis
Florence, David W. ..... Minneapolis
Flory, W. Daniel ..... Minneapolis
Fluegel, John O. ..... Minneapolis
Foker, Leslie W. ..... Minneapolis
Foley, Robert R. ..... Minneapolis
‡ Foley, William A. ..... Minneapolis
‡ Folsom, Louis B. ..... Minneapolis
Forbes, Edward F. ..... Minneapolis
† Ford, W. Harold ..... Hopkins
Fortuny, Ignacio E. ..... Minneapolis
Foss, Donald L. ..... Minneapolis
‡ Foster, Orley W. ..... Minneapolis
‡ Fox, James Rogers ..... Edina
‡ Fraley, Elwin E. ..... Minneapolis
‡ Frane, Donald B. ..... Minneapolis
‡ Frane, Gerald T. ..... Minneapolis
‡ Fredlund, Jon S. ..... Anoka
‡ Freeman, Craig W. ..... Minneapolis
Freeman, Donald W. ..... Minneapolis
French, Lyle A. ..... Minneapolis
‡ Frey, Richard J. ..... Minneapolis
Friberg, Joseph B. ..... Minneapolis
Fried, Louis A. ..... Minneapolis
† Friedell, Aaron ..... Minneapolis
Friedell, George ..... Minneapolis
‡ Friedman, Harry S. ..... Minneapolis
‡ Friend, Charles A. ..... Minneapolis
‡ Frost, John B. ..... Minneapolis
‡ Fruchtman, Stanley A. ..... Minneapolis
‡ Frys, Russell N. ..... Minneapolis
Fuglestad, Edson V. ..... Minneapolis
‡ Fuglestad, J. Roald ..... Minneapolis
† Fuller, Alice H. ..... Minneapolis
†‡ Funk, Victor K. ..... Hopkins
Furman, L. Christine ..... Minneapolis
Gaard, Richard C. ..... Robbinsdale
‡ Galbraith, Richard F. ..... Minneapolis
Galejs, Aina ..... St. Paul
Gallagher, Larry J. ..... Mound
‡ Gallett, Lester E. ..... Minneapolis
† Galligan, Margaret Mary D. ..... Minneapolis
Galway, Charles F. ..... Minneapolis
Gamble, William G. ..... Minneapolis
‡ Gannon, Paul G. ..... Minneapolis
‡ Garamella, Joseph J. ..... Minneapolis
Garetz, Floyd K. ..... Minneapolis
‡ Garske, George L. ..... Minneapolis
Garten, Joseph L. ..... Minneapolis
‡ Garvey, James T. ..... Minneapolis
Gasik, Joseph M. ..... Minneapolis
Gaviser, David ..... Minneapolis
Geis, LeRoy F. ..... Minneapolis
Geller, Joseph ..... Minneapolis
Gendron, Joseph L. ..... Minneapolis
Gentry, William C., Jr. ..... Minneapolis
George, Vane P., Jr. ..... Le Sueur
Gerster, Paul W. ..... Anoka
Gesundheit, Sim ..... Minneapolis
Gibbs, Robert W. ..... Minneapolis
‡ Giebenhain, John N. ..... Minneapolis
†‡ Giere, Joseph C. ..... Minneapolis
† Giere, Richard W. ..... Minneapolis
Gilbert, Maurice G. ..... Minneapolis
Gilbertsen, A. Sigrid ..... Minneapolis
Gilbertsen, Victor A. ..... Minneapolis
Gilles, Paul J. ..... Minneapolis
† Gingold, Benjamin A. ..... Minneapolis
Glaeser, John H. ..... Minneapolis
‡ Godfrey, H. Wilson ..... Minneapolis
‡ Goehl, Reinhold O., Jr. ..... Minneapolis
Goetz, Frederick C. ..... Minneapolis
Gokcen, Barbara W. ..... Minneapolis
Gokcen, Muharrem ..... Minneapolis
† Goldberg, Isadore M. ..... Minneapolis
Goldberg, Marvin E. ..... Minneapolis
‡ Goldberg, Stanley M. ..... Minneapolis
Goldfarb, Benjie L. ..... Minneapolis
‡ Goldfarb, Mace G. ..... Minneapolis
†‡ Goldman, Theodore I. ..... Minneapolis
‡ Goldner, Meyer Z. ..... Minneapolis
Goldstein, Alan L. ..... Hopkins
Goltz, Robert W. ..... Minneapolis
‡ Good, Gary ..... Minneapolis
‡ Goodale, Robert L., Jr. ..... Minneapolis
‡ Goodchild, William R. ..... Minneapolis
Gordon, John R. ..... Minneapolis
‡ Gordon, Sewell S. ..... Minneapolis
Gozum, Ekrem ..... Minneapolis
Grados, Carlos ..... Coon Rapids
Grage, Theodor ..... Minneapolis
Graham, John J. ..... Minneapolis
‡ Granquist, Richard D. ..... Minneapolis
‡ Grant, James B. ..... Minneapolis
Grant, Suzanne ..... Minneapolis
† Gratzek, Frank R. ..... Anoka
† Gray, Royal C. ..... Minneapolis
Greden, John F. ..... Silver Springs, MD
Green, Clayton R. ..... Excelsior
Green, Robert A. ..... Minneapolis
Greenberg, Albert J. ..... Minneapolis
‡ Greene, Leonard H. ..... Minneapolis
Greenfield, Irving ..... Minneapolis
¶ Greisheimer, Esther M. ..... Philadelphia, PA
† Grimes, Marian ..... Minneapolis
Grimmell, Francis J. ..... Minneapolis
£ Grismer, Jerome T. ..... Wauwatosa, WI
Grossling-Freudenberg, Sergio ..... Minneapolis
Grossling, Higinia C. ..... Minneapolis
Grube, David W. ..... Minneapolis
‡ Gruys, Robert I. ..... Edina
‡ Guerrero, Rafael A. ..... Minneapolis
Gullickson, Glenn, Jr. ..... Minneapolis
‡ Gunlaugson, Frederick G. ..... Minneapolis
‡ Gustafson, Paul O. ..... Minneapolis
Gustafson, Robert W. ..... Mound
‡ Gustason, Harold T. ..... Minneapolis
‡ Gustilo, Ramon B. ..... Minneapolis
Haas, John W. ..... Minneapolis
* Haberer, Helen R. ..... Stacy
‡ Haberle, Charles A. ..... Minneapolis
‡ Hagen, Kristofer ..... Minneapolis
‡ Hagen, Wayne S. ..... Minneapolis
‡ Haglin, John J. ..... Minneapolis
‡ Hakim, Ali A. ..... Minneapolis
‡ Hall, Arthur M. ..... Minneapolis

Hennepin County Medical Society *(Continued)*

‡ Hall, Harry B. .....Minneapolis
‡ Hall, Loren J. .....Minneapolis
‡ Hall, Wendell H. .....Minneapolis
Hambidge, Gove, Jr. .....Minneapolis
Hamel, Arnold L. .....Minneapolis
‡ Hamel, Joseph I. .....Minneapolis
Hammerstrom, Robert N. .....Minneapolis
‡ Handler, Seymour .....Minneapolis
Hanisch, Edward C., Jr. .....Minneapolis
†‡ Hansen, Cyrus O. .....Minneapolis
†‡ Hansen, Erling W. .....Minnetonka
† Hansen, Olga S. .....Minneapolis
‡ Hansen, Rollin M. .....Mineapolis
‡ Hanske, Edward A. .....Minneapolis
Hanson, A. Stuart .....Minneapolis
‡ Hanson, Harlow J. .....Minneapolis
Hanson, Harold B. .....St. Paul
‡ Hanson, Harold W. .....Minneapolis
*† Hanson, Henry V. .....Green Valley, AZ
*†‡Hanson, Malcolm B. .....Osseo
‡ Hanson, Mark C. L. .....Minneapolis
Hanson, Mildred S. .....Minneapolis
‡ Hanson, Stephen L. .....Minneapolis
† Hanson, William A. H. .....Minnetonka
Hanson, William B. .....Minneapolis
Harris, Leon D. .....Bloomington
Harrison, William C. .....Minneapolis
Hart, Terril H. .....Wayzata
Harkness, Donald P. .....Minneapolis
‡ Hartig, Paul R. .....Minneapolis
Hartman, Evelyn E. .....Minneapolis
‡ Hartwig, John A. .....Minneapolis
Harty, Jerome L. .....Fridley
Harvey, Clyde B. .....Minneapolis
‡ Hass, Frederick M. .....Minneapolis
‡ Hastings, Donald W. .....Minneapolis
‡ Hauge, Erling T. .....Minneapolis
‡ Haugen, George W. .....Minneapolis
Haugen, John A. .....Minneapolis
‡ Hauser, Donald C. .....Minneapolis
‡ Havel, Robert J. .....Minneapolis
‡ Haven, Walter K. .....Minneapolis
† Hawkinson, Raymond P. .....Minneapolis
‡ Hay, Lyle J. .....Minneapolis
‡ Hays, Albert T. .....Minneapolis
‡ Haywa, E. William .....Minneapolis
†‡ Head, Douglas P. .....Minneapolis
‡ Hebbel, Robert .....Minneapolis
‡ Hedrick, William L. .....Minneapolis
‡ Heinz, John N. .....Minneapolis
£ Heithoff, Kenneth B. .....Richfield
Helgaas, Steffen A. .....Farmington
Heller, Ben I. .....Minneapolis
Heller, Steven A. .....Minneapolis
‡ Hempel, Dean J. .....Minneapolis
‡ Henrikson, Earl C. .....Minneapolis
‡ Hensley, Manuel .....St. Paul
† Herbert, Willis L. .....Minneapolis
‡ Hess, Carroll N. .....Minneapolis
‡ Heupel, Hermann W. .....Minneapolis
‡ Hewitt, Marshall I. .....Minneapolis
Hiatt, John A. .....Minneapolis
Hickok, David F. .....Minneapolis
‡ Hildebrandt, Walter C. .....Minneapolis
‡ Hilgedick, William R. .....Minneapolis
Hilgermann, George .....Minneapolis
‡ Hill, David L. .....Minneapolis
‡ Hill, Earl .....Minneapolis
‡ Hill, Elmer M. .....Minneapolis
‡ Hiller, Bruce H. .....Minneapolis
‡ Hitchcock, Claude R. .....Minneapolis
‡ Hodges, Kenneth V. .....Minneapolis
‡ Hoffert, Henry E. .....Minneapolis
‡ Hoffman, Neil R. .....Minneapolis
† Hoffman, Roy A. .....Minneapolis
‡ Hoffman, Walter Lees .....Minneapolis
‡ Hofmann, Gerald N. .....Minneapolis
‡ Holm, Donald F. .....Minneapolis
‡ Holmberg, Conrad J. .....Minneapolis
Holzapfel, Fred C. .....Minneapolis
‡ Hopperstad, J. Jerome .....Minneapolis
‡ Hoppes, Emerson E. .....Minneapolis
‡ Horecki, Henry .....Minneapolis
Horns, Howard L. .....Minneapolis
‡ Horns, Norman .....Minneapolis
‡ Horns, Richard C. .....Minneapolis
Horowitz, Arthur J. .....Minneapolis
Hoseth, Wayne L. .....Minneapolis
House, James H. .....Minneapolis
‡ Householder, James R. .....Minneapolis
Hovland, Melvin L. .....Minneapolis
‡ Hovland, Richard D. .....Minneapolis
† Howard, Richard J. .....Edina
Howard, Robert B. .....Minneapolis
Howard, Solomon E. .....Minneapolis
‡ Howell, Carter W. .....Minneapolis
‡ Howell, John L. .....Minneapolis
‡ Hoyt, C. Sherman .....Minneapolis
‡ Huff, John S. .....Minneapolis
‡ Hulteng, Donald B. .....Fridley
Hung, Jui-Sung .....Minneapolis
‡ Hurr, Maland C. .....Minneapolis
‡ Hustad, Edward G. .....Minneapolis
‡ Hymes, Alan C. .....Minneapolis
† Hymes, Charles .....Minneapolis
Ide, Arthur W., Jr. .....Minneapolis
‡ Idstrom, Linneus G. .....Minneapolis
‡ Indeck, Walter .....Minneapolis
Ingalls, Edgar G. .....Minneapolis
‡ Iverslie, Philip C. .....Minneapolis
Iverson, Eleanor B. .....Minneapolis
‡ Iverson, Rolf M. .....Minneapolis
‡ Jackson, J. Albert .....Minneapolis
Jackson, Richard L. .....Minneapolis
‡ Jacobson, Leslie W. .....Minneapolis
Jacobson, Loren J. .....Minneapolis
Jacobson, Wyman E. .....St. Louis Park
‡ Jacoby, John S. .....Minneapolis
‡ Jaffe, Manuel O. .....Minneapolis
‡ Janda, George W. .....Minneapolis
Jarvis, Mary B. .....Minneapolis
Jay, Alan R. .....Temple, TX
‡ Jefferies, William L. .....Minneapolis
‡ Jensen, Nathan K. .....Minneapolis
‡ Jensen, Paul A. .....Minneapolis
Jensen, Reynold A. .....Minnetonka
Jepson, William W. .....Minneapolis
Jerome, Bourne .....Minneapolis
Jerome, Elizabeth B. K. .....Minneapolis
‡ Jeub, Robert P. .....Minneapolis
Johnson, Alan R. .....Minneapolis
Johnson, Angelo G. .....Minneapolis
‡ Johnson, Arthur B. .....Minneapolis
Johnson, Bradley D. .....Minneapolis

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Hennepin County Medical Society *(Continued)*

Johnson, Curtis A. ....Minneapolis
Johnson, David R. ....Minneapolis
‡ Johnson, Donald A. ....Minneapolis
‡ Johnson, Edward A. ....Minneapolis
‡ Johnson, Frank E. ....Minneapolis
‡ Johnson, Gordon E. ....Minneapolis
‡ Johnson, Harry A., Jr. ....Minneapolis
†‡ Johnson, James A. ....Minneapolis
‡ Johnson, John W. ....Minneapolis
† Johnson, Norman P. ....Minneapolis
Johnson, Norman Paul ....St. Paul
† Johnson, Norton T. ....Minneapolis
‡ Johnson, Paul E. ....Wayzata
‡ Johnson, Reinald G. ....Minneapolis
‡ Johnson, Richard S. ....Minneapolis
‡ Johnson, Richard V. ....Minneapolis
‡ Johnson, Robert E. ....Minneapolis
‡ Johnson, Thomas H., Jr. ....Minneapolis
Johnson, Youbert T. ....Minneapolis
‡ Johnston, Donald K. ....Minneapolis
Jones, David G. ....Minneapolis
†‡ Jones, Herbert W., Jr. ....Minneapolis
‡ Jones, Richard H. ....Minneapolis
Joransen, James A. ....Minneapolis
Jordan, Donald V. ....Minneapolis
‡ Jorgensen, Harlan ....Minneapolis
Judd, Allen S. ....Minneapolis
‡ Judd, Walter H. ....Washington, DC
Jurdy, Mitchell J. ....Minneapolis
Kadesky, Harold B. ....Minneapolis
Kaiser, Harold B. ....Minneapolis
Kalb, Thomas J. ....Minneapolis
†‡ Kallestad, Leonard L. ....Wayzata
Kane, Dennis J. ....Minneapolis
Kane, Morton C. ....Minneapolis
Kane, William J. ....Minneapolis
‡ Kaplan, Arnold P. ....Minneapolis
‡ Kaplan, J. Jacob ....Minneapolis
‡ Kaplan, Martin B. ....Minneapolis
‡ Karleen, Conrad I. ....Minneapolis
‡ Karlen, Markle ....Minneapolis
‡ Kasper, Robert E. ....Minneapolis
‡ Katkov, Harold ....Minneapolis
Katz, Beni ....Minneapolis
Katz, Harry I. ....Minneapolis
Kaye, Dale R. ....Minneapolis
Kegel, James F. ....Minneapolis
†‡ Kelby, Gjert M. ....Minneapolis
‡ Kelly, John C. ....Minneapolis
‡ Kelly, John P. ....Minneapolis
‡ Kelly, John T. ....Minneapolis
Kelly, William D. ....Minneapolis
Kennedy, Bryl J. ....Minneapolis
† Kennedy, Claude C. ....Minneapolis
‡ Khorsand, Darius ....Minneapolis
‡ Kieffer, Stephen A. ....Minneapolis
Kim, Mark K. ....Minneapolis
Kimmel, George C. ....Minneapolis
Kind, Allan C. ....Minneapolis
† King, Frances W. ....Minnetonka
‡ Kinney, William N. ....St. Paul
‡ Kiser, Joseph C. ....Minneapolis
Kjellsen, Douglas L. ....Minneapolis
‡ Kleven, Lowell H. ....Minneapolis
‡ Knapp, Miland E. ....Minneapolis
†‡ Knight, Ralph T. ....Minneapolis
† Knight, Ray R. ....Minneapolis
‡ Knobloch, William H. ....Minneapolis
Knowles, Richard A. ....Coon Rapids
Knudsen, Helen L. ....Minneapolis
Kohlhase, Robert E. ....Minneapolis
Kolars, Charles P. ....Minneapolis
† Koller, Hermann M. ....Minneapolis
*† Koller, Louis R. ....Minneapolis
Koller, Robert L. ....Minneapolis
Koontz, Peter S. ....Minneapolis
Koos, Gerald W. ....Minneapolis
Korchik, John P. ....Minneapolis
Koropchak, Nicholai ....Minneapolis
£ Koshnick, Robert A. ....Minneapolis
‡ Kostich, Nikola D. ....Minneapolis
Kottke, Frederic J. ....Minneapolis
† Koucky, Rudolph W. ....Sagle, ID
‡ Kovack, Freeman D. ....Minneapolis
‡ Kozak, Michael J. ....Minneapolis
‡ Krafft, Walter E. ....Minneapolis
‡ Kragh, Lyle V. ....Minneapolis
Kramer, Daniel W. ....Minneapolis
‡ Kremen, Arnold J. ....Minneapolis
Krieser, Albert E. ....Minneapolis
Krystosek, Lee A. ....Minneapolis
† Kucera, Frank J. ....Hopkins
† Kucera, William J. ....Santa Barbara, CA
‡ Kump, Warren L. ....Minneapolis
Kuslich, Stephen D. ....Minneapolis
Kusz, Clarence V. ....Minneapolis
‡ Kyllo, John E. ....Minneapolis
‡ Kyllonen, Ronald R. ....Minneapolis
L'Heureux, Philippe R. ....Minneapolis
LaBree, John W. ....Minneapolis
‡ Lagaard, Sheldon M. ....Minneapolis
Lai, Charles C. Y. ....Minneapolis
† Lajoie, John M. ....Minneapolis
‡ Lamb, H. Douglas ....Minneapolis
Lane, Jerald P. ....Minneapolis
Lang, Leonard A. ....Minneapolis
Langer, Leonard O., Jr. ....Minneapolis
‡ Lannon, James B. ....Minneapolis
†‡ Lapierre, Arthur P. ....Minneapolis
‡ Larsen, Frank W. ....Minneapolis
‡ Larson, Allen K. ....Minneapolis
Larson, Arthur K. ....Minneapolis
Larson, Carol Ann ....Minneapolis
‡ Larson, Donald M. ....Minneapolis
‡ Larson, Ernest J., Jr. ....Minneapolis
Larson, F. Wilmer ....Minneapolis
‡ Larson, Lawrence M. ....Minneapolis
Larson, Loren J. ....Minneapolis
‡ Larson, Richard E. ....Minneapolis
‡ Larson, Roger C. ....Minneapolis
Larson, Wyllis G. ....Minneapolis
Latts, Elliot M. ....Minneapolis
Lauritzen, Herbert ....Minneapolis
† LaVake, Rae T. ....Minneapolis
‡ Lavender, Dick R. ....St. Louis Park
Lawrence, Van S. ....Minneapolis
Lawrow, John W. ....Minneapolis
Lawson, Warren R. ....Minneapolis
‡ Lawton, James J., Jr. ....Minneapolis
Laxdal, Stefan D. ....Minneapolis
Layer, James M. ....Minneapolis
Leavenworth, Richard O., Jr. ....Minneapolis
Lee, Ju Hao ....Minneapolis
‡ Leemhuis, Andrew J. ....Minneapolis
‡ Lees, David C. ....Minneapolis
‡ Leiferman, Robert J. ....Minneapolis
Leighton, John S. ....Minneapolis

Hennepin County Medical Society *(Continued)*

Leinonen, Wendla E. ..... Anoka
Lenz, Bernard W. ..... Minneapolis
‡ Lenz, Oa ..... Minneapolis
‡ Leonard, Samuel ..... Minneapolis
Lerner, A. Ross ..... Minneapolis
‡ Leslie, Loren R. ..... Minneapolis
Leslie, W. Robert ..... Minneapolis
Lester, Theodore H. ..... Minneapolis
Letson, Robert D. ..... Minneapolis
‡ Levine, Howard M. ..... Minneapolis
Levine, Norman D. ..... Minneapolis
† Levitan, Alexander A. ..... Minneapolis
‡ Levitt, Seymour H. ..... Minneapolis
Levy, Michael ..... Minneapolis
Lewis, F. Bruce ..... Minneapolis
Lewis, Glenn M., Jr. ..... Minneapolis
‡ Lick, Louis C. ..... Minneapolis
Liebhaber, Henia F. ..... Anoka
Lillehei, James P. ..... Minneapolis
Lillehei, Richard C. ..... Minneapolis
‡ Limbeck, Donald A. ..... Minneapolis
Lindall, Arnold W., Jr. ..... Marine-on-St. Croix
Lindberg, Evan F. ..... Minneapolis
‡ Lindberg, Vernon L. ..... Minneapolis
‡ Lindberg, Winston R. ..... Minneapolis
‡ Lindeland, Arthur T. ..... Minneapolis
‡ Lindemann, Charles E. ..... Minneapolis
‡ Linderholm, Bruce E. ..... Minneapolis
‡ Lindgren, Russell C. ..... Minneapolis
Lindseth, Esten O. ..... Excelsior
‡ Linner, John H. ..... Minneapolis
‡ Linner, Paul W. ..... Minneapolis
Lipschultz, Oscar ..... St. Louis Park
Litman, Abraham B. ..... Minneapolis
‡ Litman, Thomas ..... Minneapolis
Lober, Paul H. ..... Minneapolis
‡ Locke, Murray S. ..... Minneapolis
Lofsness, Stanley V. ..... Minneapolis
Loken, Merle K. ..... Minneapolis
‡ Long, Donlin M. ..... Minneapolis
‡ Lott, Frederick H. ..... Minneapolis
† Lovett, Beatrice R. ..... Minnetonka
Lowe, Douglas A. ..... Minneapolis
Lowry, Jeanette K. ..... Minneapolis
Lowry, Paul T. ..... Minneapolis
‡ Luckey, William T. ..... Minneapolis
‡ Lueck, Wallace W. ..... Minneapolis
†‡ Lufkin, Nathaniel H. ..... Minneapolis
Lukinac, Charles J. ..... Minneapolis
Lund, George W. ..... Minneapolis
Lund, Nancy R. ..... Minneapolis
‡ Lund, Richard R. ..... Minneapolis
‡ Lundblad, Rodger R. ..... Minneapolis
*† Lundblad, Roy A. ..... Minneapolis
Lundblad, Stanley W. ..... Minneapolis
† Lundeberg, Karl R. ..... Minneapolis
Lundquist, Charles B. ..... Minneapolis
‡ Lundquist, Virgil J. P. ..... Minneapolis
‡ Lynch, Michael F. ..... Minneapolis
Lyon, Fred A. ..... Minneapolis
Lyon, John D. ..... Hopkins
Lysne, Richard B. ..... Minneapolis
‡ Lysyj, Anatol ..... Minneapolis
Lyzenga, Anton G. ..... Minneapolis
McCaffrey, F. John ..... Minneapolis
‡ McCampbell, Malcolm D. ..... Minneapolis
‡ McCannel, Malcolm A. ..... Minneapolis
† McCarthy, Donald ..... Minneapolis
McCollister, Robert J. ..... Minneapolis
‡ McCormick, Donald P. ..... Minneapolis
† McDaniel, Orianna ..... Minneapolis
† McFarland, Arthur H. ..... Minneapolis
† McGandy, Robert F. ..... Minneapolis
McGovern, Lawrence ..... Minneapolis
†‡ McInerny, Maurice W. ..... Minneapolis
† McKelvey, John L. ..... St. Paul
McKelvey, John M. ..... Minneapolis
‡ McKenzie, Charles H. ..... Minneapolis
McKhann, Charles F. ..... Minneapolis
McKinlay, Gordon L. ..... Minneapolis
‡ McKinley, C. Richard ..... Minneapolis
† McKinney, Frank S. ..... Minneapolis
McLaughlin, Byron H. ..... Minneapolis
McMahon, John E. ..... Minneapolis
McNeil, John J. ..... Minneapolis
‡ McParland, Felix A., Jr. ..... Minneapolis
*†‡ McPheeters, Herman O. ..... Minneapolis
‡ McQuoid, David W. ..... Minneapolis
MacCormick, Robert R., Jr. ..... Minneapolis
†‡ MacDonald, Daniel A. ..... Minneapolis
MacGibbon, James D. ..... Minneapolis
‡ MacKinnon, Donald C. ..... Minneapolis
†‡ Mach, Frank B. ..... Minneapolis
Mach, John R. ..... Minneapolis
Macheledt, Neil L. ..... Anoka
‡ Madsen, Donald O. ..... Minneapolis
‡ Maeder, Edward C. ..... Minneapolis
‡ Maeder, Edward C., Jr. ..... Minneapolis
‡ Magee, Timothy M. ..... Minneapolis
Mahan, Charles S. ..... Minneapolis
‡ Malmquist, Carl P. ..... Minneapolis
Mandel, Sheldon L. ..... Minneapolis
Manick, Kenneth P. ..... Minneapolis
‡ Mankey, James C. ..... Minneapolis
Mann, George A. ..... Minneapolis
‡ Manoles, Ellias N. ..... Minneapolis
Manolis, Deane C. ..... Minneapolis
£ Mantel, Fred ..... Hopkins
‡ Mark, Aaron L. ..... Minneapolis
‡ Mark, Merle S. ..... Minneapolis
‡ Mark, Peter M. ..... Minneapolis
‡ Marking, George H. ..... Minneapolis
‡ Markland, Colin ..... Minneapolis
Markovitz, Jack M. ..... Minneapolis
‡ Marte, Egon ..... Minneapolis
‡ Martin, Frank E. ..... Minneapolis
‡ Martin, George R. ..... Minneapolis
Martinson, Carl J. ..... Wayzata
Martinson, Elmer J. ..... Wayzata
‡ Maslansky, Robert A. ..... Minneapolis
‡ Massee, Joseph S. ..... Minneapolis
‡ Mastbaum, Leonard I. ..... Minneapolis
Matthews, John A. G. ..... Minneapolis
Maunder, John B. ..... Minneapolis
† Maxeiner, Stanley R. ..... Minneapolis
‡ Maxeiner, S. R., Jr. ..... Minneapolis
Mayberg, Donald M. ..... Minneapolis
Meany, Thomas J. ..... Minneapolis
Mecklenburg, Fred E. ..... Minneapolis
‡ Medina, Ambrosio M., Jr. ..... Wayzata
‡ Meeker, Henry C. ..... Minneapolis
Meekin, Patrick C. ..... Minneapolis
‡ Melichar, Paul J. ..... Minneapolis
Meller, Robert L. ..... Minneapolis
Mensheha, Nicholas M. ..... Minneapolis

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Hennepin County Medical Society *(Continued)*

‡ Merner Thomas B. ..... Minneapolis
† Merrick, Charlotte T. ..... St. Paul
Merrill, Daniel C. ..... Minneapolis
Messenheimer, Myron G. ..... Minneapolis
‡ Metz, Donald D. ..... Minneapolis
Meyer, Alvin J. ..... Minneapolis
Michael, Alfred F. ..... Minneapolis
† Michel, Henry H. ..... Minneapolis
*† Michelson, Henry E. ..... Minneapolis
† Mickelson, Emma F (Fronk) ..... Holmes Beach, FL
Middlebrook, John E. ..... Minneapolis
Miller, Gerald J. ..... Ft. Riley, KS
‡ Miller, H. Dawes ..... Minneapolis
‡ Miller, Harold E. ..... Minneapolis
‡ Miller, Hugo E. ..... Minneapolis
‡ Miller, J. Carleton ..... Minneapolis
Miller, William P. ..... Minneapolis
‡ Millett, D. Keith ..... Minneapolis
Minder, John G. ..... Minneapolis
Mindrum, Gerald G. ..... Minneapolis
Minsky, Armen A. ..... Minneapolis
‡ Mitby, Irvin L. ..... Minneapolis
‡ Mitchell, Berton D. ..... Minneapolis
Mitchell, Edward C. ..... College Place, WA
‡ Mitchell, Mancel T. ..... Minneapolis
‡ Mixer, Harry W. ..... Minneapolis
Moe, John H. ..... Minneapolis
Moe, W. Wyatt ..... Minneapolis
‡ Moehn, John T. ..... Minneapolis
† Moen, Johannes K. ..... Minneapolis
Moghaddam, Alaeddin ..... Minneapolis
‡ Monson, Einer M. ..... Minneapolis
‡ Monson, Paul S. ..... Minneapolis
Monson, Warren A. ..... Minneapolis
‡ Moody, David L. ..... Minneapolis
† Moore, Irvin H. ..... Eden Prairie
Moorhead, Marie ..... Minneapolis
Moos, Daniel J. ..... Minneapolis
‡ Moral, Harvey M. ..... Minneapolis
Moran, Leo J. ..... New Brighton
Moriarty, James A. ..... Minneapolis
Moriarty, Joseph D. ..... Coon Rapids
Mork, A. Harold ..... Anoka
‡ Mork, Frank E. ..... Anoka
‡ Mork, Frank E., Jr. ..... Minneapolis
Moss, Nyel H. ..... Minneapolis
‡ Mosser, Donn G. ..... Minneapolis
Mossman, Philip L. ..... Minneapolis
‡ Moyer, Leonard B. ..... Minneapolis
‡ Mueller, James M. ..... Minneapolis
‡ Mulholland, William M. ..... Minneapolis
‡ Mullin, Gerald T., Jr. ..... Minneapolis
‡ Mulvahill, John E. ..... Minneapolis
‡ Munkittrick, Ronald C. ..... Minneapolis
Murray, Charles L. ..... Minneapolis
† Murray, Elisabeth M. ..... Minneapolis
£ Murphy, William R. C. ..... Minneapolis
‡ Muschenheim, Frederick ..... Minneapolis
‡ Muske, Marvin M. ..... Minneapolis
‡ Musty, Nicholas J. ..... Minneapolis
Myers, Jay A. ..... Minneapolis
‡ Myhre, James ..... Minneapolis
Mylrea, Murray J. ..... Burnsville
Nagobads, Ilgvars J. ..... Minneapolis
Nagobads, V. George ..... Minneapolis
‡ Najarian, John S. ..... Minneapolis
Nash, Eldore B. ..... Minneapolis
†‡ Neal, Joe M. ..... Minneapolis
*‡ Neary, Richard P. ..... Minneapolis
† Nelson, Bernice A. ..... Minneapolis
Nelson, C. Barton ..... Minneapolis
Nelson, Carleton A. ..... Minneapolis
† Nelson, David W. ..... Minneapolis
‡ Nelson, Edward N. ..... Minneapolis
* Nelson, George E. ..... Minneapolis
‡ Nelson, Glen D. ..... Minneapolis
‡ Nelson, Gunard A. ..... Minneapolis
† Nelson, Harvey ..... Deerfield Beach, FL
‡ Nelson, Lloyd S. ..... Minneapolis
Nelson, Maxine O. ..... Minneapolis
‡ Nelson, Maynard C. ..... Minneapolis
‡ Nelson, O. L. Norman ..... Minneapolis
‡ Nelson, Wallace I. ..... Minneapolis
Nerenberg, Sidney ..... Minneapolis
Nesse, Anton S. ..... Minneapolis
‡ Nesset, Lawren B. ..... Minneapolis
‡ Nesset, William D. ..... Minneapolis
Neumann, Roland F. ..... Minneapolis
‡ Neumeister, Charles A. ..... Minneapolis
Neuwirth, Gerardo D. ..... Golden Valley
Nicholas, S. Scott, Jr. ..... Minneapolis
Nicolette, Charles C. ..... Minneapolis
Nielsen, David J. ..... Minneapolis
‡ Nilsen, John A. ..... Minneapolis
Nolan, Robert K. ..... Brooklyn Center
‡ Noran, Harold H. ..... Minneapolis
‡ Nord, Robert E. ..... Minneapolis
† Nordlie, Paul E. ..... Minneapolis
Noren, George R. ..... Minneapolis
‡ Norman, Franklin C. ..... Minneapolis
‡ Norman, Mark L., Jr. ..... Minneapolis
Norval, Mildred A. ..... Minneapolis
‡ Nuessle, William F. ..... Minneapolis
‡ Nydahl, Bruce C. ..... Minneapolis
†‡ Nydahl, Malvin J. ..... Minneapolis
‡ O'Brien, Bruce J. ..... Minneapolis
‡ O'Brien, William A. ..... Minneapolis
† O'Donnell, James E. ..... Minneapolis
‡ O'Leary, John B. ..... Minneapolis
O'Neil, Bernerd L. ..... Minneapolis
O'Hanlon, William J. ..... Minneapolis
‡ O'Phelan, E. Harvey ..... Minneapolis
Officer, Charles D. ..... Burnsville
Ohmann, Ronald J. ..... Minneapolis
Olavs, Olga ..... Minneapolis
‡ Olfelt, Paul C. ..... Minneapolis
† Olsen, E. George ..... Minnetonka
Olsen, Jay R. ..... Minneapolis
‡ Olson, Alton C. ..... Minneapolis
Olson, C. Kent ..... Minneapolis
Olson, Carl J. ..... Minneapolis
‡ Olson, Detlof M. ..... Minneapolis
‡ Olson, Duane C. ..... Minneapolis
Olson, Hardin E. ..... Minneapolis
† Olson, Olof A. ..... Minneapolis
‡ Olson, Philip A. ..... Minneapolis
‡ Olson, Robert A. ..... Minneapolis
Olson, Robert E. ..... Minneapolis
Olson, Robert W. ..... Minneapolis
Olson, Rolland A. ..... Wayzata
‡ Opheim, Richard H. ..... Minneapolis
‡ Oppen, E. Gerhard ..... Minneapolis
Oppen, Melvin G. ..... Minnetonka
Opstad, Earl T. ..... Minneapolis
‡ Orbuch, Martin W. ..... Minneapolis
‡ Orkin, Milton ..... Minneapolis
Orn, Duane L. ..... Minneapolis

Hennepin County Medical Society *(Continued)*

Osterberg, Kenneth A. ..... Minneapolis
Ostrov, Charles S. ..... Minneapolis
Ott, Eugene C. ..... Minneapolis
Owen, Richard R. ..... Minneapolis
Paal, Dwain J. ..... Minneapolis
‡ Paisner, Hyman M. ..... Minneapolis
Palen, Benjamin J. ..... Scottsdale, AZ
‡ Palm, E. Theodore ..... Minneapolis
‡ Paparella, Michael M. ..... Minneapolis
Papermaster, Ralph ..... Minneapolis
Papermaster, Theodore C. ..... St. Louis Park
Park, Wilford E. ..... Minneapolis
Parod, John D. ..... Minneapolis
‡ Parrott, John C. ..... Minneapolis
Pattee, James J. ..... Minneapolis
‡ Patterson, Paul G. ..... Minneapolis
Paule, William J. ..... Minneapolis
‡ Peluso, Charles R. ..... Minneapolis
Pennington, Mary ..... Minneapolis
‡ Peper, Martin C. ..... Minneapolis
‡ Perlman, Everett C. ..... Minneapolis
Perlman, Herschel L. ..... St. Louis Park
‡ Peteler, Jennings C. L. ..... Minneapolis
Petersen, Byron D. ..... Minneapolis
‡ Petersen, Deane A. ..... Minneapolis
‡ Petersen, Glenn L. ..... Minneapolis
‡ Petersen, William E. ..... Minneapolis
Peterson, Charles A. ..... Minneapolis
Peterson, Charles R. ..... Minneapolis
Peterson, John A. ..... Minneapolis
‡ Peterson, Oliver H., Jr. ..... Minneapolis
Peterson, Palmer A. ..... Minneapolis
‡ Peterson, Rodney H. ..... Minneapolis
‡ Peterson, Theodore A. ..... Minneapolis
‡ Peterson, Willard C., Jr. ..... Minneapolis
‡ Petit, Julien V. ..... Minneapolis
† Petit, Leon J. ..... Minneapolis
‡ Pewters, John T. ..... Minneapolis
‡ Pfohl, Richard A. ..... Minneapolis
† Phelps, Kenneth A. ..... Palo Alto, CA
Phelps, Robert D. ..... Minneapolis
Phibbs, Clifford M., Jr. ..... Minneapolis
‡ Pilling, Loran F. ..... Minneapolis
Pincus, Mitchell ..... Minneapolis
Pinell, Octavio C. ..... Chattahoochee, FL
Pizarro, Remi L. ..... Minneapolis
‡ Plasha, Matthew K. ..... Coon Rapids
Plass, Herbert F. R. ..... Minneapolis
Pleissner, Karl W. ..... Minneapolis
Plimpton, Nathan C. ..... Minneapolis
Pohl, John F. ..... Minneapolis
† Poland, Jerome D. ..... Minneapolis
Polesky, Herbert F. ..... Minneapolis
Poley, Brooks J. ..... Minneapolis
Pollak, Kurt ..... Minneapolis
‡ Pollock, Anthony J. ..... Minneapolis
†‡ Polzak, James A. ..... Roseville
† Pone, John J. ..... Minneapolis
‡ Popadiuk, Peter ..... Minneapolis
‡ Popowich, John G. ..... Minneapolis
† Poppe, Frederick H. ..... Miami, FL
Potter, Robert B. ..... Minneapolis
† Pratt, Fred J. ..... Minneapolis
‡ Prem, Konald A. ..... Minneapolis
Preston, Frank S., Jr. ..... Minneapolis
‡ Price, William E. ..... Minneapolis
‡ Prickman, William E. ..... Minneapolis
‡ Priest, Robert E. ..... Minneapolis
Proshek, Lumir C. ..... Minneapolis
‡ Quello, Robert O. B. ..... Minneapolis
Quiggle, Arthur B. ..... Minneapolis
Quist, Henry W., Jr. ..... Minneapolis
Raab, David E. ..... Minneapolis
Racer, Harley J. ..... Minneapolis
Raich, John J. ..... Minneapolis
‡ Raile, Richard B. ..... Minneapolis
£ Randall, Patricia A. ..... Minneapolis
Randall, David A. ..... Minneapolis
‡ Randall, Philip S. ..... Minneapolis
‡ Ransom, H. Robert ..... Osseo
‡ Ratelle, Alexander E. ..... Minneapolis
Recht, Thomas M. ..... Minneapolis
‡ Reece, Richard L. ..... Minneapolis
Reed, John H., Jr. ..... Minneapolis
Reed, Sheldon C. ..... Minneapolis
Regan, John J. ..... Minneapolis
‡ Rehmann, Ronald E. ..... Coon Rapids
Reichel, Samuel M. ..... Minneapolis
‡ Reif, Harold A. ..... Minneapolis
‡ Reiley, Richard E. ..... Minneapolis
‡ Reinhart, Richard O. ..... Minneapolis
Reisdorf, George E. ..... St. Louis Park
‡ Reiser, Milton P. ..... Minneapolis
£ Reller, Carl Raymond, Jr. ..... Minneapolis
‡ Remole, William D. ..... Minneapolis
Resch, Joseph A. ..... Minneapolis
Reynolds, James ..... Minneapolis
Rholl, Arnold O. ..... Minneapolis
‡ Rice, Carl O. ..... Minneapolis
Rice, Edwin G. ..... Minneapolis
Rice, Fred A. ..... Minneapolis
‡ Richardson, Robert J. ..... Minneapolis
†‡ Richdorf, Lawrence F. ..... Minneapolis
‡ Rierson, Phillip A. ..... Minneapolis
Riley, John D. ..... Minneapolis
Riordan, Elsie M. ..... Minneapolis
‡ Ripple, Rudolph J., Jr. ..... Minneapolis
‡ Risch, Ronald E. ..... Minneapolis
Rizer, Dean K. ..... Minneapolis
† Robb, Edwin F. ..... Boca Raton, FL
‡ Robbins, Owen F. ..... Minneapolis
Roberts, Byron H. ..... Minneapolis
‡ Roberts, Lewis J. ..... Minneapolis
Robinson, Cortland O. ..... Minneapolis
Rock, William H. ..... Anoka
‡ Rocknem, Robert E. ..... Minneapolis
Rockwell, Curtiss V. ..... Minneapolis
‡ Rodgers, Richard S. ..... Minneapolis
† Rohrmann, Charles A., Jr. ..... Minneapolis
Rogin, Norton ..... Minneapolis
Rollins, Pat ..... Minnetonka
Romness, Kenneth B. ..... Mound
‡ Rosenbaum, David L. ..... Minneapolis
‡ Rosendahl, Frederick G. ..... Minneapolis
† Rosenfield, Abraham B. ..... Minneapolis
Rosenow, John H. ..... Minneapolis
Rosenquist, Rudolph J. ..... Minneapolis
Rosenstein, Hanan J. ..... Minneapolis
†‡ Rosenwald, Reuben M. ..... Anoka
‡ Rossen, Ralph ..... Minneapolis
Rotenberg, Robert J. ..... Minneapolis
Rotenberg, Samuel ..... Beverly Hills, CA
‡ Rothnem, Morris S. ..... Minneapolis
Rubin, Manly ..... Minneapolis
Rucker, Thomas K. ..... Minneapolis
† Rucker, William H. ..... Minneapolis

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Hennepin County Medical Society *(Continued)*

† Rud, Norman E. ..... Edina
‡ Ruiz, Ernest ..... Minneapolis
‡ Russeth, Arthur N. ..... Minneapolis
‡ Rusten, Elmer M. ..... Minneapolis
Rydberg, John S. ..... Minneapolis
Rydland, Arne D. ..... Minneapolis
St. Cyr, Harry M. ..... Minneapolis
St. Cyr, Kenneth J. ..... Minneapolis
‡ Salchert, John J. ..... Minneapolis
‡ Saliterman, Bernard I. ..... Minneapolis
‡ Salovich, Edward L. ..... Minneapolis
‡ Salovich, Elmer R. ..... Minneapolis
Sanchez, Jose S. ..... W. St. Paul
‡ Sandt, Karl E. ..... La Jolla, CA
‡ Sanfilippo, Sylvester J. ..... Minneapolis
Sartor, Richard ..... Minneapolis
Sawyer, Glen T. ..... Minneapolis
Sayther, Keith D. ..... Minneapolis
‡ Sborov, Abe M. ..... Minneapolis
‡ Scanlan, Patrick J. ..... Minneapolis
Schaar, Frances E. ..... Minneapolis
† Schaefer, Wesley G. ..... Minneapolis
Schaffhausen, Irwin F. ..... Minneapolis
Schaffhausen, Mildred ..... Minneapolis
‡ Scherer, L. Raymond ..... Minneapolis
Scherling, Sidney S. ..... Minneapolis
‡ Schiele, Burtrum C. ..... Minneapolis
Schissel, Gregory A. ..... Minneapolis
‡ Schissel, Richard C. ..... Minneapolis
Schless, James M. ..... Minneapolis
Schmidt, W. Robert ..... Minneapolis
† Schmitt, Samuel C. ..... Fallbrook, CA
Schneck, Jack I. ..... Minneapolis
Schoening, Herbert A. ..... Minneapolis
‡ Schoenwetter, William F. ..... Minneapolis
‡ Schottler, Jerry L. ..... Minneapolis
Schottler, Max E. ..... Minneapolis
†‡ Schroeder, Albert J. ..... Minneapolis
‡ Schultz, Alan ..... Minneapolis
Schultz, Alvin L. ..... Minneapolis
‡ Schultz, J. Harold ..... Minneapolis
‡ Schultz, Peter J. ..... Minneapolis
Schultz, Robert J. ..... Minneapolis
‡ Schumacher, John W. ..... Minneapolis
† Schumacher, Robert V. ..... Minneapolis
‡ Schut, Lawrence J. ..... Minneapolis
Schwartz, E. Robert ..... Minneapolis
‡ Scott, Horace G. ..... Minneapolis
‡ Scott, Robert H. ..... Minneapolis
Scott, William R. ..... Minneapolis
† Seaberg, John A. ..... Pequot Lakes
Seay, James E., III ..... Minneapolis
Segal, Edward L. ..... Minneapolis
Segal, Martin A. ..... Minneapolis
Segal, Marvin S. ..... Minneapolis
‡ Segal, Sheldon J. ..... Minneapolis
† Seham, Max ..... St. Paul
Seifert, Gregory L. ..... Minneapolis
*† Seifert, Milton H. ..... Excelsior
‡ Seifert, Milton H., Jr. ..... Excelsior
‡ Seljeskog, Edward L. ..... Minneapolis
Semba, Thomas ..... Minneapolis
‡ Semsch, Robert D. ..... Wayzata
Severseike, Odean M. ..... Minneapolis
‡ Seymour, John L. ..... Minneapolis
Shackelford, Terry C. ..... Minneapolis
‡ Shandorf, James F. ..... Minneapolis
Shackelford, Terry C. ..... Minneapolis
† Shaperman, Eva P. ..... San Diego, CA
Shapiro, Irving ..... Minneapolis
Shapiro, Sidney K. ..... Minneapolis
‡ Shapiro, Stanley W. ..... Minneapolis
‡ Shattuck, Clark A. ..... Minneapolis
‡ Shaw, Howard A. ..... Minneapolis
Shea, Andrew W. ..... Minneapolis
‡ Shemesh, Alvin ..... Minneapolis
‡ Sher, Lewis ..... Minneapolis
‡ Sherman, Lloyd F. ..... Minneapolis
† Shillington, Maurice A. ..... Ft. Lauderdale, FL
Sholler, Lawrence J. ..... Minneapolis
Shragg, Robert I. ..... Minneapolis
Shronts, John F. ..... Minneapolis
Sidell, Franklin D. ..... Minneapolis
Siegmann, William C. ..... Minneapolis
‡ Sigel, Melvin E. ..... Minneapolis
‡ Silas, Ralph M. ..... Minneapolis
Silver, John D. ..... Minneapolis
‡ Silverstein, Paul M. ..... Minneapolis
‡ Simmons, Richard K. ..... Minneapolis
Simmons, Richard L. ..... Minneapolis
Simo, Kathleen Kay ..... Minneapolis
‡ Simonson, Donald B. ..... Minneapolis
Simso, Lee A. ..... Minneapolis
Singher, Lawrence J. ..... Minneapolis
‡ Sinykin, Melvin B. ..... Minneapolis
Sipe, James W. ..... Coon Rapids
Skjold, Arthur C. ..... Minneapolis
‡ Sletten, Richard G. ..... Minneapolis
‡ Slosser, Gaius, J., II ..... Minneapolis
Smiley, John T. ..... Minneapolis
†‡ Smisek, Frank M. ..... Minneapolis
† Smith, Adam M. ..... Minneapolis
‡ Smith, Archie M. ..... Minneapolis
Smith, Barlow ..... Minneapolis
‡ Smith, Baxter A., Jr. ..... Minneapolis
‡ Smith, Graham G. ..... Minneapolis
Smith, Henry T. ..... Minneapolis
‡ Smith, John E. ..... Minneapolis
Smith, Nadine G. ..... Minneapolis
‡ Smith, Theodore S. ..... Minneapolis
‡ Soderberg, Richard J. ..... Minneapolis
†‡ Soderlind, Ragnar T. ..... Minneapolis
‡ Soiseth, Robert P. ..... Minneapolis
‡ Solhaug, Samuel B., Jr. ..... Minneapolis
Soll, Robert W. ..... Minneapolis
Solvason, Harold M. ..... Minneapolis
‡ Spano, Joseph P. ..... Minneapolis
‡ Spencer, Bernard J. ..... Minneapolis
Spencer, David L. ..... Anoka
Spink, Wesley W. ..... Minneapolis
‡ Sponsel, Kenath H. ..... Minneapolis
‡ Stahr, Aubrey C. ..... Hopkins
Standefer, James E. ..... Minneapolis
† Stanford, Charles E. ..... Elcho, WI
‡ Steidl, Richard M. ..... Minneapolis
†‡ Stelter, Lloyd A. ..... Minneapolis
† Stenstrom, Annette T. ..... Grand Marais
Stenzel, Donald A. ..... Minneapolis
Stenzel, Joseph A. ..... Minneapolis
Stephens, William E. ..... Minneapolis
Sterrie, Norman A. ..... Minneapolis
Stevens, Sheridan S. H. ..... Minneapolis
Stewart, Marvin J. ..... Minneapolis
Stewart, Paul B. ..... Minneapolis
‡ Stiegler, Farrell S. ..... Minneapolis
‡ Stillman, M. Thomas ..... Minneapolis
Stolee, Curtis N. ..Republique Malgeche, Madagascar

Hennepin County Medical Society *(Continued)*

‡ Stoltz, Robert C. ..... Minneapolis
‡ Stone, Norman F. ..... Minneapolis
Stone, Stanley P. ..... Minneapolis
Strait, Herbert S. ..... Minneapolis
‡ Strand, Clarence M. ..... Minneapolis
‡ Strand, Peter J. ..... Minneapolis
† Strand, Richard C. ..... Bloomington
Streu, Richard E. ..... Minneapolis
‡ Strickler, Jacob H. ..... Minneapolis
Strobel, Jack L. ..... Minneapolis
‡ Strom, Gordon W. ..... Minneapolis
‡ Strom, Robert L. ..... Minneapolis
‡ Stromgren, Delph T. ..... Minneapolis
Stromme, William B. ..... Minneapolis
Strunk, Clarence A. ..... Minneapolis
‡ Student, Richard E. ..... Minneapolis
‡ Sturges, Robert L. ..... Minneapolis
Subak, Barbara H. ..... Minneapolis
‡ Subby, Walter ..... Minneapolis
Sukov, Marvin ..... Minneapolis
‡ Sulciner, Aurel ..... Minnetonka
‡ Sundberg, A. Bruce ..... Minneapolis
‡ Sutherland, John E. ..... Minneapolis
Swaiman, Kenneth F. ..... Minneapolis
‡ Swallen, Thomas O. ..... Minneapolis
†‡ Swanson, David A. ..... Minneapolis
Swanson, Gerald E. ..... Minneapolis
‡ Swanson, John O. ..... Minneapolis
Swanson, Wallace L. ..... Richfield
†‡ Sweetser, Horatio B. ..... Minneapolis
‡ Sweetser, Theodore H., Jr. ..... Minneapolis
‡ Swendseen, Carl J. ..... Minneapolis
Swenson, James D. ..... Minneapolis
‡ Swenson, Richard W. ..... Minneapolis
Swift, Dean C. ..... Minneapolis
Symchych, Boris E. ..... Minneapolis
‡ Tam, Ernest C. ..... Minneapolis
‡ Tambornino, Joseph M. ..... Minneapolis
Tanaka, Shin ..... Minneapolis
‡ Tangen, George V. ..... Minneapolis
† Taylor, Joseph H. ..... Ft. Lauderdale, FL
‡ Tchou, Mien-Fa ..... Minneapolis
‡ Telander, Robert L. ..... Minneapolis
tenBensel, Robert W. ..... Minneapolis
‡ Tenner, Robert J. ..... Minneapolis
‡ Teska, Byron A. ..... Minneapolis
‡ Teynor, Joseph W. ..... Minneapolis
‡ Tharp, Ralph ..... Minneapolis
Thelemann, Arthur R., Jr. ..... Minneapolis
Theobalt, Inge M. ..... Minneapolis
‡ Theologides, Anthanasios ..... Minneapolis
Thomas, William H. ..... Minnetonka
Thomasson, Robert D. ..... Minneapolis
Thompson, Arthur ..... Minneapolis
Thysell, Desmond M. ..... Minneapolis
Tierney, Jon P. ..... Minneapolis
Titrud, Leonard A. ..... Minneapolis
‡ Tobin, John A. ..... Minneapolis
Tobin, John D. ..... Minneapolis
Torres, Fernando ..... Minneapolis
† Town, Louise A. ..... Minneapolis
Townes, C. Dwight, Jr. ..... Minneapolis
Trach, Benedict B. ..... Minneapolis
Treat, William A. ..... Minneapolis
Trost, Francis J. ..... Minneapolis
‡ Trow, James E. ..... Minneapolis
Tsai, Shih Hao ..... Minnetonka
‡ Tucker, Richard C. ..... Minneapolis
Tudor, Richard B. ..... Minneapolis
£ Tully, Timothy E. ..... Minneapolis
Turbak, Charles E. ..... Minneapolis
‡ Turkbas, Nejat ..... Minneapolis
‡ Twidwell, Joseph E. ..... Minneapolis
Ulrich, Wesley D. ..... Bethesda, MD
‡ Ulvestad, Harold S. ..... Minneapolis
‡ Utendorfer, Robert W. ..... Minneapolis
‡ Vaaler, Robert T. ..... Minneapolis
‡ Valgemae, Romil ..... Minneapolis
Van Oppen, Dirk J. A. ..... Minneapolis
Vellek, Donald G. ..... Minneapolis
‡ Verby, John E. ..... Minneapolis
Vik, A. Elliott ..... Minneapolis
Vilaseca, Louis B. ..... Minneapolis
‡ Von Drashek, Stanley C. ..... Minneapolis
von Weiss, David L. ..... Minneapolis
Vorlicky, Loren N. ..... Minneapolis
Wagner, Christian J. ..... Minneapolis
‡ Wagner, Robert M. ..... Minneapolis
† Waldron, Carl W. ..... Scottsdale, AZ
‡ Waldron, John F. ..... Minneapolis
Walker, Fredric E., Jr. ..... Minneapolis
Wall, Carl R. ..... Minneapolis
‡ Wallinga, Jack V. ..... Minneapolis
† Walonick, Albert L. ..... Hopkins
Walsh, John G. ..... Minneapolis
Wang, Josef K. ..... Minneapolis
† Wangensteen, Owen H. ..... Minneapolis
Ward, A. Neal ..... Minneapolis
‡ Warren, John W. ..... Minneapolis
Watson, C. Gordon ..... Minneapolis
Watson, Cecil J. ..... Minneapolis
Wattenberg, Lee W. ..... Minneapolis
‡ Weatherhead, D. Stuart P. ..... Minneapolis
‡ Webb, Edgar A. ..... Minneapolis
Webber, Richard J. ..... Minneapolis
‡ Weber, Lowell W. ..... Minneapolis
Weisberg, Martin G. ..... Minneapolis
Weisberg, Rapheal J. ..... Minneapolis
Weisel, Mary R. ..... Minneapolis
‡ Wendland, John P. ..... Minneapolis
Wengler, Robert A. ..... Minneapolis
† Werges, Thomas M. ..... Minneapolis
Werner, George ..... Minneapolis
‡ Wesolowski, Stanley ..... Minneapolis
† West, Catherine C. ..... Edina
Wester, Mary Sue ..... Minneapolis
Westgate, Hugh D. ..... Minnetonka
† Wetherby, Macnider ..... Minneapolis
Wethington, Joseph F. ..... Coon Rapids
‡ Wett, Richard J. ..... Minneapolis
Wexler, Harold M. ..... Minneapolis
‡ Wheeler, Robert W. ..... Minneapolis
Whitacre, John C., II ..... Minneapolis
White, Asher A. ..... Minneapolis
† White, Willard D. ..... Edina
Whitesell, Lloyd A. ..... Minneapolis
‡ Widen, Wilford F. ..... Minneapolis
Wigdahl, Lowell C. ..... Minneapolis
‡ Wigdahl, Luther O. ..... Minneapolis
Wigg, Norman P. ..... Minneapolis
‡ Wilcox, William A. ..... Minneapolis
Wild, John J. ..... Minneapolis
*† Wilder, Kenneth W. ..... Minneapolis
*† Wilder, Robert L. ..... Minneapolis
† Wilder, Russell M., Jr. ..... Topeka, KS
‡ Wilder, Walter L. ..... Minneapolis
†‡ Wilken, Paul A. ..... Minneapolis

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Hennepin County Medical Society *(Continued)*

†‡ Williams, Henry L. ..... West St. Paul
‡ Williams, Paul A. ..... Minneapolis
‡ Williams, Richard E. ..... Robbinsdale
Wilson, John A. ..... Minneapolis
‡ Wilson, Robert E. ..... Minneapolis
‡ Wilson, Thomas M., Jr. ..... Minneapolis
Winchell, Paul ..... Minneapolis
Winter, Laurence E. ..... Minneapolis
† Winther, Nora M. C. ..... Columbus, OH
‡ Wippermann, Frederic F. ..... Minneapolis
‡ Wisiol, Erich S. ..... Minneapolis
Wisness, Osmund A. ..... Savage
Woellner, Richard C. ..... Minneapolis
†‡ Wohlrabe, Arthur A. ..... Minneapolis
‡ Wohlrabe, A. Cabot ..... Minneapolis
‡ Wohlrabe, Robert G. ..... Minneapolis
‡ Wolter, Frederick H. ..... Minneapolis
Wong, Edward T. ..... Minneapolis
Wong, Howard H. ..... Bloomington
Woodbury, John W. ..... Minneapolis
Woodley, Donald W. ..... Minneapolis
‡ Worrell, Philip J. ..... Minneapolis
‡ Woyda, William C. ..... Minneapolis
Wright, Donald L. ..... Minneapolis
Wright, Francis S. ..... Minneapolis
Wright, William S. ..... Minneapolis
Wuest, Frederick C. ..... Wayzata
† Wynne, Herbert M. N. ..... Wayland, MA
Yeager, Terrell F. ..... Anoka
Yelle, Matthew D. ..... Anoka
†‡ Ylvisaker, Ragnvald S. ..... Minneapolis
Yonehiro, Earl G. ..... Minneapolis
Young, Ronald C. ..... Minneapolis
Yue, Alexander ..... Minneapolis
Yue, Wen Y. ..... Excelsior
Zahrendt, O. Lewis ..... Minneapolis
Zak, Solomon J. ..... Minneapolis
‡ Zaworski, Leo A. ..... Minneapolis
‡ Zelickson, Alvin S. ..... Minneapolis
† Zierold, Arthur A. ..... Minneapolis
‡ Zinn, Charles W. ..... Wayzata
‡ Zinter, Ferdinand A. ..... Minneapolis

LYON-LINCOLN COUNTY MEDICAL SOCIETY

Lyon and Lincoln Counties
Regular meetings, 6 meetings—Spring and Fall
Annual meeting, November
Number of members 23

PRESIDENT
Mulder, Richard ..... Ivanhoe

SECRETARY
Kaczrowski, William ..... Marshall
‡ Bosley, Patrick ..... Balaton
‡ Eckdale, John E. ..... Marshall
*†‡Ford, Burton C. ..... Marshall
‡ Hedenstrom, Philip C. ..... Marshall
†‡ Johnson, C. Percy ..... Tyler
‡ Kaczrowski, William ..... Marshall
† Kreuzer, Titus C. ..... New Brighton
Lee, Norman J. ..... Tracy
‡ Monson, Leonard J. ..... Canby
‡ Mueller, LeRoy E. ..... Hendricks
‡ Mulder, Richard D. ..... Ivanhoe
‡ Murphy, Joseph E. ..... Marshall
‡ Myers, John W. ..... Canby
‡ Odland, Olin M. ..... Marshall
‡ Olson, Robert T. ..... Canby
‡ Panning, Wayne P. ..... Marshall
‡ Peterson, Kenneth A. ..... Marshall
† Rohrer, Christian A. ..... Madison Lake
Stein, Robert L. ..... Tyler
‡ Stover, Laddie E. ..... Marshall
‡ Taintor, Ronald W. ..... Marshall
Tan, Ruby ..... Marshall
‡ Thompson, Carl O. ..... Hendricks
† Workman, Warner G. ..... Tracy
† Yaeger, Wilbert W. ..... Torrance, CA

McLEOD COUNTY MEDICAL SOCIETY

McLeod County
Regular meetings, third Thursday of each month
Annual meeting, November
Number of members 16

PRESIDENT
Jensen, Alvin M. ..... Brownton

SECRETARY
Selmo, Joseph D. ..... Norwood
Blackwell, Leonard ..... Jackson
Bretzke, Carl O. ..... Hutchinson
‡ Close, Gerald A. ..... Glencoe
Griebie, Grant L. ..... Hutchinson
Hegrenes, Robert L. ..... Hutchinson
Huebert, Dan W. ..... Hutchinson
‡ Jensen, Alvin M. ..... Brownton
Kleinkauf, Thomas P. ..... Hutchinson
* Lippmann, Elmer W. ..... Hutchinson
McNeil, Maurice R. ..... Glencoe
Navratil, Donald R. ..... Glencoe
Peterson, Kenneth H. ..... Hutchinson
Selmo, Joseph D. ..... Norwood
Smith, George R. ..... Hutchinson
‡ Smyth, John J. ..... Lester Prairie
‡ Stifter, A. J. ..... Winsted
‡ Truesdale, Clark W. ..... Glencoe

MID-MINNESOTA MEDICAL SOCIETY

Kandiyohi, Meeker, Redwood, Renville and Swift
Regular meetings, third Thursday of each month
Annual meeting in November
Number of members 74

PRESIDENT
Guy, Jack ..... New London
SECRETARY
Malone, Patrick M. ..... Willmar
Allison, David D. ..... Litchfield
‡ Anderson, Chester A. ..... Hector
† Anderson, Richard E. ..... Willmar
Bergstrom, John G. ..... Cokato
Bosland, Howard G. ..... Rochester
Brace, Ray I. ..... Willmar
Ceplecha, S. Francis ..... Redwood Falls
Chunn, Stanley S. ..... Willmar
Cosgriff, James A., Jr. ..... Olivia
Danielson, Lennox ..... Litchfield
Dille, Donald E. ..... Litchfield
Docksey, John W. ..... Willmar
Dreyling, Roger A. ..... Eden Valley
Dunstan, Paul L. ..... Willmar
Eberley, Tobe S. ..... Benson
Eichelberger, Dale L. ..... Willmar
Ellinger, Albert J. ..... Willmar
† Fawcett, Arthur M. ..... Renville
Fedders, Skaidrite C. ..... Willmar
Fedor, Robert D. ..... Spicer
Flinn, James B. ..... Redwood Falls
† Frederickson, Alice C. ..... Willmar
Furr, Leo O. ..... Bird Island
Gaebe, Milton B. ..... Clara City
† Giere, Silas W. ..... Benson
‡ Gilman, Lloyd C. ..... Willmar
Griffin, Richard P. ..... Benson
Guy, Jack A. ..... New London
Hazen, Richard W. ..... Willmar
Hetzler, John A. ..... Willmar
‡ Hinderaker, Harris P. ..... Willmar
Hinz, Walter E. ..... Willmar
Hodapp, Robert V. ..... Willmar
Houts, Joseph C. ..... Dassel
Jacobs, Douglas L. ..... Willmar
Johnson, Daniel A. ..... Litchfield
Kaminski, Gregory W. ..... Redwood Falls
Kaufman, Edward J. ..... Appleton
Lackore, Leonard K. ..... Willmar
Larrabee, Walter F. ..... Willmar
Leitch, Cecil ..... Litchfield
Lenz, Joseph R. ..... Morton
McAfee, David K. ..... Willmar
McCarthy, Austin M. ..... Willmar
† Macklin, William E., Jr. ..... Litchfield
Maitland, Edwin T. ..... Willmar
Malone, Patrick M. ..... Willmar
Mattson, A. D. ..... Willmar
Mattson, Donald S. ..... Willmar
Meinert, John K. ..... Willmar
Michels, Roger P. ..... Willmar
Munneke, Lyle ..... Clara City
‡ Nelson, Glenn E. ..... Redwood Falls
Nolan, William A. ..... Litchfield
Olson, Gregory M. ..... Litchfield
Opsahl, Lawrence J. ..... Willmar
Petersen, Donald H. ..... Willmar
Peterson, Willard E. ..... Willmar
‡ Proeschel, Ray K. ..... Willmar
Robinson, William W. ..... Agana, Guam
Robnik, Spencer L. ..... Willmar
Roem, Joseph A. ..... Appleton
Ruchie, Warren H. ..... Willmar
Ruhe, Albert H. ..... Willmar
Rygh, Harold N. ..... Atwater
Sadd, Milton F. ..... Willmar
Salter, Wilson M. ..... Willmar
Schnell, Frederick S. ..... Litchfield
Smith, Lloyd A. ..... Willmar
Strand, Roger W. ..... Willmar
‡ Strauchler, John ..... Belview
Thompson, Russell A. ..... Willmar
‡ Wagner, Norman W. ..... Benson
Wilmot, Cecil A. ..... Litchfield
† Wilmot, Harold E. ..... Litchfield

MOWER COUNTY MEDICAL SOCIETY

Mower County
Regular meetings, last Friday of the month
Annual meeting, November
Number of members 32

PRESIDENT
Hagen, John D. ..... Austin
SECRETARY
Todd, John C. ..... Austin
‡ Anderson, David P., Jr. ..... Austin
‡ Anderson, Harold J. ..... Austin
†‡ Cronwell, Bernhard J. ..... Austin
‡ Hagen, John D. ..... Austin
† Hertel, Garfield E. ..... McAllen, TX
‡ Hesla, Inman A. ..... Austin
‡ Isele, Reginald H. ..... Austin
† Leck, Paul C. ..... Palm Desert, CA
‡ Lommen, M. L. ..... Austin
Lommen, Peter A., Jr. ..... Austin
† McKenna, Jay K. ..... LaJolla, CA
‡ Miller, Herman ..... Austin
‡ Mlinar, Joseph P. ..... Austin
† Morse, Morton P. ..... LeRoy
Morse, Roger D. ..... LeRoy
‡ Muchow, Gene C. ..... Austin
‡ Nesse, James A. ..... Austin
‡ O'Rourke, William J. ..... Austin
‡ Patten, John C. ..... Austin
‡ Pesonen, Clifford A. ..... Austin
‡ Roberts, George A. ..... Austin
† Robertson, Paul A. ..... Austin
‡ Seery, Thomas M. ..... Austin
† Smythe, Gwendolyn S. ..... Austin
‡ Stahl, G. W. ..... Austin
‡ Taufic, Mansur ..... Austin
† Thomson, James M. ..... Austin
‡ Todd, John C. ..... Austin
Trudeau, David ..... Austin
‡ Twiggs, Leo F. ..... Austin
‡ Van Cleve, H. P., Jr. ..... Austin
‡ Wright, Robert R. ..... Austin

NICOLLET-LeSUEUR COUNTY MEDICAL SOCIETY

Nicollet and LeSueur Counties
Regular meetings, first Monday of even months
Annual meeting, December
Number of members 19

PRESIDENT
Engstrom, George ..... St. Peter
SECRETARY
Walden, A. Don ..... LeSueur
‡ Anderson, Jo E. ..... LeSueur
Brink, Donald ..... St. Peter
‡ Engstrom, George E. ..... St. Peter
‡ Grimes, Burton P. ..... St. Peter
† Haes, Julius E. ..... St. Peter
† Hiniker, Peter J. ..... St. Peter
Koskela, L. E. ..... St. Peter
† Larson, Milo H. ..... St. Peter
†‡ Lenander, Mellvin E. L. ..... St. Peter
‡ Olmanson, Edmund G. ..... St. Peter
‡ Olmanson, M. Donald ..... St. Peter
‡ Olmanson, Vern ..... St. Peter
Sauer, Jean C. ..... Ft. Snelling
‡ Sheppard, Charles G. ..... St. Peter
‡ Sjostrom, Lawrence E. ..... St. Peter
‡ Sonnesyn, Nels N. ..... LeSueur
‡ Strathern, Carleton S. ..... St. Peter
Thompson, A. Henry ..... St. Peter
Walden, A. Don ..... LeSueur
† Wohlrabe, Clarence F. ..... North Mankato

PARK REGION DISTRICT AND COUNTY MEDICAL SOCIETY

Douglas, Grant, Otter Tail and Wilkin Counties
Regular meetings, March, June, September and December
Annual meeting, December
Number of members 63

PRESIDENT
Hom, Leong Y. ..... Fergus Falls
SECRETARY
Syverson, Leslie A. ..... Fergus Falls
Akhavan, Traz H. ..... Alexandria
† Arndt, Harry W. ..... Detroit Lakes
Baker, Jeannette L. ..... Fergus Falls
Baker, Norman H. ..... Fergus Falls
‡ Bateman, Clarence V. ..... Fergus Falls
Boline, Clifford A. ..... Battle Lake
Cain, James H. ..... Alexandria
Carlson, Carl E. ..... Alexandria
‡ Carlson, Homer J. ..... Pelican Rapids
Clifford, George W. ..... Alexandria
‡ Colman, Edward L. ..... Fergus Falls
‡ Daehlin, Rolf ..... Fergus Falls
‡ Doms, Vernon A. ..... Elbow Lake
Emerson, Edwin E. ..... Osakis
Engebretson, Paul ..... Alexandria
‡ Estrem, Ralph L. ..... Fergus Falls
Estrem, Robert D. ..... Fergus Falls
Geiser, Peter M. ..... Alexandria
Green, John F. ..... Alexandria
‡ Heegaard, William G. ..... Alexandria
†‡ Helseth, Hovald K. ..... Fergus Falls
‡ Hom, Leong Y. W. ..... Fergus Falls
† Houkom, Bjarne ..... Fergus Falls
Hunt, Kai K. ..... Alexandria
‡ Jacobson, Clifford W. ..... Breckenridge
‡ Kevern, Jay L. ..... Henning
‡ Kippen, Neil ..... Breckenridge
‡ Korda, Henry A. ..... Pelican Rapids
Kreiser, Robert D. ..... Fergus Falls
Kuhlmann, Vernon G. ..... Alexandria
Larson, Dorette W. ..... Fergus Falls
‡ Lewis, Charles W. ..... Henning
‡ Lu, Cheng-en ..... Fergus Falls
‡ Luh, Edwin F. ..... Fergus Falls
Lu, Jennie W. G. ..... Fergus Falls
Lueders, James ..... Evansville
‡ Mathison, Larry A. ..... Fergus Falls
*† Mortensen, Nels G. ..... St. Paul
‡ Mouritsen, Glenn J. ..... Fergus Falls
Myhre, John H. ..... Fergus Falls
Nelson, Roy A. ..... Fergus Falls
‡ Ness, Richard A. ..... Fergus Falls
‡ Nicholson, Richard W. ..... Fergus Falls
‡ O'Brien, Louis T. ..... Breckenridge
‡ Orandi, Ahmad ..... Fergus Falls
‡ Orandi, Mehdi ..... Fergus Falls
† Ostergaard, Erling ..... Elbow Lake
Perkins, Douglass E. ..... Alexandria
‡ Pulido, Ernesto ..... Fergus Falls
Reinhardt, James H. ..... Alexandria
‡ Richter, Paul H. ..... Fergus Falls
‡ Rockwood, Philo H. ..... Fergus Falls
‡ Sanderson, David J. ..... Fergus Falls
Schoeneberger, P. B. ..... Perham
‡ Shaver, Ward ..... Fergus Falls
Stemsrud, Harold L. ..... Alexandria
Struthers, Lewis ..... Parkers Prairie
‡ Syverson, Leslie A. ..... Fergus Falls
† Tanquist, Edwin J. ..... Alexandria
Tanquist, Edwin J., Jr. ..... Alexandria
Trajano, Lorenzo F. ..... Fergus Falls
Undem, Dale ..... Alexandria
Warner, James J. ..... Perham
Wasson, Loren F. ..... Alexandria

RAMSEY COUNTY MEDICAL SOCIETY

Ramsey County
Regular meetings, last Monday each month except
June, July and August
Annual meeting in January
Number of members 634

PRESIDENT
Martin, Dwight L. ..... St. Paul
SECRETARY
Johnson, Herbert W. ..... St. Paul
EXECUTIVE SECRETARY
Aldean, Mrs. Sue ..... St. Paul

Abrams, Alexander, Jr. ..... St. Paul
Adair, Albert F., Jr. ..... St. Paul
Adams, Harold R. ..... St. Paul
Adcock, Leon L. ..... St. Paul
Ahlstrom, Robert C. ..... St. Paul
‡ Ahrens, Robert M. ..... St. Paul
‡ Albrecht, Raymond ..... St. Paul
‡ Alden, John F. ..... St. Paul
‡ Altman, Robert L. ..... St. Paul
‡ Alton, Donald G. ..... St. Paul
‡ Amerongen, Werner W. ..... St. Paul
‡ Anderson, Dale L. ..... St. Paul
‡ Anderson, David W. ..... St. Paul
Anderson, James J. ..... St. Paul
Anderson, Margaret C. ..... St. Paul
‡ Anderson, Richard W. ..... St. Paul
‡ Antolak, Stanley J., Jr. ..... St. Paul
‡ Arny, Frederick D. ..... St. Paul
† Arny, Frederick P. ..... St. Paul
Ashmore, Herbert C. ..... St. Paul
Asp, Donald S. ..... St. Paul
Ault, Lynn L. ..... St. Paul
‡ Auran, David B. ..... St. Paul
‡ Aurelius, J. Richards ..... St. Paul
‡ Ausman, Duane R. ..... St. Paul
‡ Austrian, Sol ..... St. Paul
‡ Baab, Gary H. ..... St. Paul
‡ Babb, Frank S. ..... St. Paul
Bach, Jerome M. ..... Minneapolis
‡ Bah, Merle C. ..... St. Paul
‡ Baker, C. Robert, Jr. ..... St. Paul
‡ Balce, Regino V. ..... St. Paul
Bauer, Eugene L. ..... St. Paul
‡ Beck, Charles J. ..... North St. Paul
Beckman, Donovan L. ..... St. Paul
‡ Beek, Harvey O. ..... St. Paul
‡ Beer, John J. ..... St. Paul
‡ Bellomo, James ..... St. Paul
Belsito, Alphonso A. ..... St. Paul
‡ Belz, Reinmar ..... St. Paul
Benthack, Elaine M. ..... Minneapolis
‡ Bergh, Allen V. ..... St. Paul
‡ Bernier, M. J. ..... St. Paul
† Bernstein, William C. ..... St. Paul
‡ Bieter, Thomas G. ..... St. Paul
Birkebak, Roland C. ..... St. Paul
Bjornson, Robert G. B. ..... St. Paul
*† Black, Earl J. ..... St. Paul
Blackburn, Henry W. ..... St. Paul
‡ Blomberg, William R. ..... St. Paul
Blumberg, Henry B. ..... St. Paul
† Bock, Rolland A. ..... St. Paul
Boies, Lawrence R., Jr. ..... St. Paul
Bonello, Frank J. ..... St. Paul
† Bouma, Lewis R. ..... St. Paul
‡ Brainard, John B. ..... St. Paul
Breen, John J. ..... St. Paul
* Briggs, John F. ..... St. Paul
‡ Briggs, Thomas G. ..... White Bear Lake
Broadie, Thomas E. ..... St. Paul
Brockberg, Daryl G. ..... St. Paul
£ Brockberg, James A. ..... St. Paul
† Brodie, Walter D. ..... St. Paul
‡ Broman, Harold R., Jr. ..... North St. Paul
Brown, Charles T. ..... St. Paul
‡ Brown, Christopher J. ..... St. Paul
‡ Brown, Hector M. ..... St. Paul
Brown, James E., Jr. ..... St. Paul
‡ Brown, James P. ..... St. Paul
‡ Brown, John M. ..... St. Paul
‡ Bruhl, Martin G. ..... St. Paul
‡ Bulinski, Theodore J. ..... St. Paul
‡ Burklund, Edwin C. ..... St. Paul
Burlingame, David A. ..... St. Paul
*‡ Burmeister, Richard O. ..... St. Paul
‡ Burns, John M. ..... St. Paul
‡ Burton, J. Richard ..... St. Paul
‡ Bush, Robert P. ..... St. Paul
Butwinick, Conrad S. ..... St. Paul
Byrne, William J. ..... St. Paul
‡ Cain, Clark L. ..... St. Paul
Campion, Brian C., Jr. ..... St. Paul
‡ Capistrant, Terrance D. ..... St. Paul
‡ Carley, Richard B. ..... St. Paul
Cass, Alexander S. ..... St. Paul
‡ Castle, Donald D. ..... St. Paul
Cedarleaf, Cherry B. ..... White Bear Lake
† Chatterton, Carl C. ..... St. Paul
‡ Clark, W. Bruce ..... St. Paul
Cleary, John ..... St. Paul
‡ Cochrane, Byron B. ..... St. Paul
Coddon, Walter D. ..... St. Paul
† Colby, Woodward L. ..... St. Paul
Cole, Wallace H. ..... St. Paul
‡ Coleman, John B. ..... St. Paul
‡ Colton, Roger S. ..... St. Paul
‡ Comfort, Thomas H. ..... St. Paul
‡ Connolly, Coleman J. ..... St. Paul
‡ Connolly, Joseph P. ..... South St. Paul
† Connor, Charles E. ..... St. Paul
Cooper, Charles C. ..... Moose Lake
Cooper, Jack M. ..... St. Paul
† Countryman, Roger S. ..... Saratoga, CA
‡ Craig, David M. ..... St. Paul
‡ Cram, Barclay M. ..... St. Paul
‡ Cramer, Glen G. ..... New Brighton
Crowley, James H. ..... St. Paul
‡ Crudo, Vincent D. ..... St. Paul
‡ Crum, Arthur Z. ..... St. Paul
Crutchfield, Charles E. ..... St. Paul
Crutchfield, Susan E. ..... St. Paul
‡ Culligan, David E. ..... St. Paul
‡ Culligan, John A. ..... St. Paul
‡ Culver, Lucian G. ..... St. Paul
‡ Cumming, Edward D. ..... St. Paul
‡ Daly, Alfred E. ..... St. Paul
‡ Damberg, Sheldon W. ..... St. Paul

Continued on Next Page

Ramsey County Medical Society *(Continued)*

‡ Davis, Edward V. ....St. Paul
Davis, Eunice R. A. ....St. Paul
‡ Derauf, Donald E. ....St. Paul
‡ Derechin, William ....St. Paul
‡ Deters, Donald C. ....St. Paul
Dickinson, Paul B. ....St. Paul
Dieperink, Willem ....St. Paul
†‡ Dittrich, Raymond J. ....St. Paul
Dolmage, George H. ....St. Paul
§ Donehower, Ross C. ....St. Paul
‡ Dooley, Robert T. ....St. Paul
Duerr, Eleanor E. ....St. Paul
‡ Duffy, John L. ....St. Paul
‡ Dunham, Charles K. ....St. Paul
‡ Dunn, James P. ....St. Paul
Dunn, Robert C. ....St. Paul
‡ Durkin, John L. ....St. Paul
‡ Duthoy, Everette J. ....St. Paul
‡ Duvall, Arndt J., III ....St. Paul
Drydal, Paul J. ....St. Paul
*† Earl, George A. ....St. Paul
‡ Earl, John R. ....St. Paul
† Edwards, J. Willard ....St. Paul
‡ Edwards, Jesse E. ....St. Paul
Edwards, Laura E. ....St. Paul
Edwards, Lloyd G. ....St. Paul
£ Edwards, Richard B. ....St. Paul
Edwards, Thomas J. ....St. Paul
Edwardson, Phillip L. ....St. Paul
‡ Eelkema, Herman H. ....St. Paul
Eginton, Charles T. ....Fargo, ND
‡ Eilers, Vincent E. ....St. Paul
Ellis, Ronald W. ....St. Paul
Elumba, Teodoro V. ....St. Paul
† Emerson, Edward C. ....St. Paul
‡ Emmons, Robert W. ....St. Paul
† Endress, Edward K. ....St. Paul
‡ England, Rodney W. ....St. Paul
‡ Enroth, Oscar E. ....St. Paul
Erickson, Donald L. ....St. Paul
Erlanson, A. Cornell ....St. Paul
‡ Erling, Carl B. ....St. Paul
‡ Ersfeld, Murray P. ....St. Paul
‡ Farr, John D. ....St. Paul
‡ Fee, John G. ....St. Paul
‡ Felder, Davitt A. ....St. Paul
‡ Felion, Arthur J. ....St. Paul
Ferguson, John N. ....St. Paul
† Fesler, Harold H. ....West St. Paul
‡ Fink, Daniel L. ....St. Paul
‡ Fischer, Robert F. ....St. Paul
‡ Flannery, Hubert F. ....St. Paul
Fleming, Janice L. ....St. Paul
Flom, Reynold P. ....St. Paul
‡ Flom, Robert S. ....St. Paul
Florence, David W. ....St. Paul
‡ Flynn, Louis L., Jr. ....St. Paul
†‡ Fogelberg, Emil J. ....St. Paul
‡ Foreman, Richard T. ....St. Paul
Forsythe, James R. ....St. Paul
Fox, LeRoy J. ....St. Paul
‡ Freeman, Charles D., Jr. ....St. Paul
Fritz, Wallace L. ....St. Paul
†‡ Froats, Charles W. ....St. Paul
Frost, John W. ....St. Paul
‡ Frye, Charles W. ....St. Paul
‡ Fuller, Benjamin F. ....White Bear Lake
Funke, Joyce L. ....St. Paul
‡ Gaertner, Frank M. J., Jr. ....St. Paul
‡ Gaertner, John R. ....St. Paul
‡ Galligan, John J. ....St. Paul
‡ Gardner, Walter P. ....St. Paul
† Garrow, Douglas M. ....St. Paul
Gaute, Svend T. ....St. Paul
‡ Gedgaudas, Eugene ....St. Paul
†‡ Gehlen, Joseph N. ....St. Paul
Geist, Robert W. ....St. Paul
Gibbs, Edward C. ....St. Paul
‡ Gilchrist, Milton R. ....St. Paul
Gillespie, Delmar R. ....St. Paul
‡ Gilsdorf, Donald A. ....St. Paul
‡ Glenny, William R. ....St. Paul
Goetz, Frederick C. ....Minneapolis
Goldberg, Robert J. ....St. Paul
‡ Goldsmith, Joseph W. ....St. Paul
Goodman, Ernest ....St. Paul
‡ Goott, Bernard ....St. Paul
†‡ Govrik, Kalman ....St. Paul
‡ Gretsch, Gerald A. ....St. Paul
Gridley, John W. ....St. Paul
‡ Griffin, Patrick J. ....St. Paul
*‡ Griffin, Thomas M. ....St. Paul
‡ Gruninger, Robert P. ....St. Paul
‡ Gudio, Felix A., Jr. ....St. Paul
‡ Gumnit, Robert J. ....St. Paul
Guthrie, J. Cameron ....St. Paul
#‡ Haight, James W. ....Ft. Snelling
Hakanson, Erick Y. ....St. Paul
‡ Hall, Barnard ....St. Paul
‡ Hammes, Ernest M., Jr. ....St. Paul
‡ Hannon, Donald W. ....St. Paul
‡ Hanton, Edward M. ....St. Paul
Harmon, Gaius E. ....St. Paul
Harris, Boyd L. ....St. Paul
Harris, John E. ....Minneapolis
‡ Harris, Max E. ....St. Paul
† Hartfiel, William F. ....St. Paul
Hartig, Marjorie ....St. Paul
Haus, Erhard ....St. Paul
‡ Hauser, Charles W. ....St. Paul
†‡ Hauser, Victor P. ....St. Paul
‡ Hawkinson, Harlan W. ....St. Paul
‡ Hayes, Albert F. ....St. Paul
†‡ Heck, William W. ....St. Paul
‡ Hedenstrom, Charles W. ....St. Paul
† Hedenstrom, Frank G. ....St. Paul
‡ Hedenstrom, Richard H. ....St. Paul
† Hedlund, Charles J. ....St. Paul
Heimel, Albert J. ....St. Paul
‡ Henderson, Terrance P. ....White Bear Lake
† Hengstler, William H. ....St. Paul
‡ Henke, Wilbert J. ....St. Paul
‡ Henry, James S. ....St. Paul
† Herman, Samuel M. ....St. Paul
‡ Herrick, Donald W. ....St. Paul
‡ Hilger, Jerome A. ....St. Paul
‡ Hilger, Laurence D. ....St. Paul
Hilgers, Robert D. ....Tenafly, NJ
‡ Hilker, Marcus D. ....St. Paul
Hill, Charlotte W. ....St. Paul
Hinckley, Robert G. ....White Bear Lake
† Hiniker, Louis P. ....St. Paul
‡ Hippchen, Ray C. ....St. Paul
‡ Ho, Shu Kang ....St. Paul
‡ Hodgson, Corrin H. ....St. Paul
Hodgson, Jane E. ....St. Paul
‡ Hohmann, Albert ....St. Paul

Ramsey County Medical Society *(Continued)*

Hollinshead, William H. .....St. Paul
†‡ Holt, John E. .....St. Paul
Hopkins, G. Wendell .....Minneapolis
‡ Hottinger, George C. .....St. Paul
Houle, Rollin J. .....St. Paul
Houlton, William H. .....St. Paul
Howe, Newell W. .....West St. Paul
Hunt, Vincent R. .....Minneapolis
‡ Hunter, Samuel W. .....St. Paul
‡ Hurwitz, Milton M. .....St. Paul
‡ Huseby, Thomas L. .....St. Paul
‡ Husebye, Kjeld O. .....St. Paul
Ireland, Gerald W. .....St. Paul
‡ Jackson, William C. .....St. Paul
‡ James, Ellery M. .....St. Paul
‡ James, John W. .....St. Paul
‡ Janecek, James, ...New Brighton
‡ Janssen, Martin E. .....St. Paul
Jarvis, Charles W. .....St. Paul
‡ Jastram, Rupert M. .....St. Paul
Johnson, Carl E. .....St. Paul
Johnson, Carolyn A. .....St. Paul
‡ Johnson, Daniel T. .....St. Paul
‡ Johnson, Herbert W. .....St. Paul
Johnson, Lyle O. .....St. Paul
‡ Johnson, Richard J. .....St. Paul
Johnson, Robert H. .....St. Paul
‡ Johnson, Rodger L. .....St. Paul
‡ Johnson, Thomas E. .....St. Paul
Jorgensen, Donald R. .....St. Paul
Joseph, Arnold H. .....St. Paul
‡ Kantar, Yale C. .....St. Paul
Kaplan, David H. .....Edina
Karon, Everett H. .....St. Paul
‡ Karon, Irvine M. .....St. Paul
‡ Kasper, Eugene M. .....St. Paul
Katz, Louis J. .....Long Beach, CA
Keenan, Thomas P. .....St. Paul
Kelly, Edward H. .....St. Paul
Kelly, Helen M. .....Cottage Grove
‡ Kelly, Joseph R. .....St. Paul
‡ Kelsey, Chauncey M. .....St. Paul
*†‡Kenefick, Emmett V. .....St. Paul
‡ Kenyon, Thomas J. .....St. Paul
† Kesting, Herman .....St. Paul
Kleinsasser, Warren L. .....St. Paul
Kluge, John W. .....St. Paul
‡ Knowles, Roy C. .....St. Paul
Knutson, Gehard E. .....St. Paul
Knutson, Robert C. .....St. Paul
Kodres, Nina .....St. Paul
Koelz, Thomas A. .....St. Paul
‡ Kosiak, Michael .....St. Paul
Koza, Donald W. .....St. Paul
‡ Kramer, James D. .....St. Paul
‡ Krezowski, Thomas K. .....St. Paul
‡ Kugler, Alex A. .....St. Paul
‡ Kuske, Albert W. .....St. Paul
‡ Kusske, Bradley W. .....St. Paul
‡ Kusske, Douglas R. .....St. Paul
‡ Kvam, Lowell L. .....St. Paul
Lade, Roswith I. .....St. Paul
LaFave, James W. .....St. Paul
‡ Lampert, Ronald M. .....St. Paul
‡ Lane, Miles I. .....White Bear Lake
‡ Lannin, Bernard G. .....St. Paul
‡ Lannin, Donald R. .....St. Paul
Larkin, John E. .....St. Paul
Larson, Eva Jane Ostergren .....St. Paul
‡ Larson, Jerrold V. .....St. Paul
† Laszewski, Franz Von Zelberschwecht .....St. Paul
‡ Lawler, Kevin M. .....St. Paul
Layman, Thomas E. .....St. Paul
‡ Leach, Clifford G. .....St. Paul
Leahy, Dennis M. .....St. Paul
‡ Lees, Jack R. .....St. Paul
Lehman, Donald S. .....St. Paul
‡ Leick, Richard M. .....St. Paul
† Leitch, Archibald .....South St. Paul
Leonard, Stanley .....St. Paul
‡ Lerdahl, Kenneth .....St. Paul
Lerner, Irving, J. .....St. Paul
Lessard, Richard J. .....St. Paul
Leven, N. Logan .....St. Paul
‡ Leverenz, Carleton W. .....St. Paul
Levitan, Leonard H. .....St. Paul
Levitt, George X. .....St. Paul
Lewis, Joyce S., Jr. .....St. Paul
‡ Lick, William J. .....St. Paul
‡ Lien, Richard J. .....St. Paul
† Lightbourn, Edgar L. .....Hastings
‡ Lilleberg, Norbert J. .....St. Paul
Lillemoen, Roger D. .....Minneapolis
‡ Lillie, Andrew R. .....St. Paul
‡ Lindell, Robert E. .....St. Paul
‡ Lindquist, Max F. .....South St. Paul
* Lippman, Hyman S. .....St. Paul
Litkewitsch, Helene .....St. Paul
† Lobell, Michael .....St. Paul
‡ Loken, Selmer M. .....St. Paul
Lowe, Alexander D. .....West St. Paul
† Lowe, Thomas A. .....South St. Paul
‡ Lufkin, Murray W. .....St. Paul
†‡ Lundholm, Arthur M. .....Princeton
Lunseth, John B. .....St. Paul
‡ Lunzer, Richard G. .....St. Paul
‡ Lynch, Francis W. .....St. Paul
‡ Lynch, Raymond P. .....St. Paul
‡ Lynch, Richard P. .....St. Paul
‡ McBride, John W. .....St. Paul
‡ McCafferty, Charles W. .....St. Paul
McCain, Donovan L. .....St. Paul
‡ McCarthy, Charles J. .....St. Paul
McClellan, Robert J. .....St. Paul
McCloud, C. Naumann .....St. Paul
‡ McEllistrem, Edward J. .....St. Paul
‡ McEllistrem, Gerald D. .....St. Paul
‡ McEwan, Alexander .....St. Paul
‡ McGroarty, Brian J. .....St. Paul
‡ McHutchinson, Samuel K. .....St. Paul
McKenzie, Eva E. .....St. Paul
McLeod, John A. .....St. Paul
‡ McNeill, John A. .....St. Paul
Mackoff, Sam M. .....Phoenix, AZ
† Madland, Robert S. .....St. Paul
Malerich, J. Anthony, Jr. .....Cottage Grove
‡ Manlove, Charles H., Jr. .....St. Paul
‡ Marta, John B. .....St. Paul
‡ Martin, Dwight L. .....St. Paul
Mateo, Guillermo .....St. Paul
* Matthews, James H. .....Minneapolis
Matus, Richard N. .....St. Paul
‡ Mazzitello, William F. .....St. Paul
‡ Mears, Burtis J. .....St. Paul
‡ Medelman, John P. .....St. Paul

Continued on Next Page

Ramsey County Medical Society *(Continued)*

‡ Melancon, Joseph F. ..... St. Paul
Melich, Paz C. ..... River Falls, WI
‡ Merrick, Robert L. ..... St. Paul
Messenger, Michael A. ..... St. Paul
‡ Michienzi, Leonard J. ..... St. Paul
‡ Miller, Albert G. ..... St. Paul
Miller, Fletcher A. ..... St. Paul
Miller, Winston R. ..... St. Paul
Miller, Zondal R. ..... St. Paul
‡ Milnar, Frank J. ..... St. Paul
Milroy, Thomas W. ..... Ann Arbor, MI
‡ Mishek, Charles J. ..... St. Paul
‡ Mitchell, George S. ..... St. Paul
† Molander, Herbert A. ..... St. Paul
‡ Moller, Jurgen J. ..... West St. Paul
‡ Monahan, Robert H. ..... St. Paul
‡ Mooney, Robert D. ..... St. Paul
Moren, J. Adelaide ..... St. Paul
‡ Mowlem, Albert ..... St. Paul
Mulford, Beatrice ..... St. Paul
‡ Muller, A. Eugene ..... North St. Paul
Mundahl, Harold R. ..... St. Paul
Murphy, Jack T. ..... St. Paul
‡ Myaya, Po ..... St. Paul
* Nauth, Bernard S. ..... Minneapolis
‡ Neher, Frederick J. ..... St. Paul
‡ Neira, Edward H. ..... St. Paul
£ Nelson, David J. ..... St. Paul
‡ Nelson, Delbert R. ..... St. Paul
‡ Nelson, Loren E. ..... St. Paul
‡ Nelson, Louis A. ..... St. Paul
Nelson, Robert P. ..... St. Paul
‡ Nelson, Ronald J. ..... St. Paul
Nesvacil, Leon ..... St. Paul
‡ Nichols, Thomas O. ..... St. Paul
£ Nimlos, Kenneth O. ..... St. Paul
£ Nimlos, Lenore O. ..... St. Paul
Norman, David D. ..... St. Paul
Norquist, Joseph L. ..... St. Paul
† Nye, Lillian L. ..... St. Paul
O'Brien, Gerald R. ..... Minneapolis
‡ O'Brien, John C. ..... St. Paul
‡ O'Kane, Thomas W. ..... St. Paul
‡ O'Malley, Valentine ..... St. Paul
‡ O'Neill, Nial C. ..... St. Paul
† O'Reilley, Bernard E. ..... Sun City, AZ
Ockuly, Orville E. ..... St. Paul
† Ogden, Warner ..... River Falls, WI
† Ohage, Justus ..... St. Paul
‡ Olsen, Ralph L. ..... St. Paul
Olson, Barbara F. ..... Minneapolis
‡ Osekowsky, Henry J. ..... St. Paul
‡ Ouellette, Alfred ..... St. Paul
‡ Owens, Frederick M., Jr. ..... St. Paul
‡ Palm, Neil M. ..... St. Paul
‡ Paulson, Elmer C. ..... St. Paul
‡ Paulson, Wallace J. ..... St. Paul
Peake, Janna Zoe ..... St. Paul
† Pearson, Fritz R. ..... St. Paul
‡ Pearson, Malcolm M. ..... St. Paul
† Pedersen, Arthur H. ..... St. Paul
‡ Pelletier, Rene W. ..... St. Paul
‡ Perry, John F., Jr. ..... St. Paul
£ Petersen, Kenneth ..... Portland, OR
‡ Peterson, Donald H. ..... St. Paul
‡ Peterson, Edward A. ..... St. Paul
‡ Peterson, Harold O. ..... Minneapolis
*† Peterson, Joel L. E. ..... St. Paul
‡ Peterson, Roy L. ..... White Bear Lake
Phillips, Leonard ..... St. Paul
‡ Pilney, Frank T. ..... St. Paul
Plotke, Harry L. ..... St. Paul
Polski, Paul G. ..... South St. Paul
‡ Post, Edmund A. ..... St. Paul
‡ Powers, Robert L. ..... St. Paul
Prentice, Walter B. ..... Fort Snelling
‡ Proud, Harry S. ..... St. Paul
Quast, John E. ..... St. Paul
Quattlebaum, Frank W. ..... St. Paul
‡ Raaen, Olaf J. ..... St. Paul
Rabcevich, Anatole ..... St. Paul
‡ Ralph, James R. ..... St. Paul
Ramlow, Ralph M. ..... West St. Paul
† Ramsey, Walter R. ..... St. Paul
‡ Raths, Otto N., Jr. ..... St. Paul
£ Rauenhorst, John M. ..... St. Paul
‡ Ravits, Harold G. ..... St. Paul
‡ Rea, Charles E. ..... St. Paul
Redleaf, Paul D. ..... St. Paul
Reif, Robert W. ..... St. Paul
‡ Richardson, Edward J., Jr. ..... St. Paul
‡ Rick, Paul F. W. ..... St. Paul
‡ Rinkey, Eugene ..... St. Paul
† Ripple, Rudolph J. ..... St. Paul
†‡ Ritt, Albert E. ..... St. Paul
Roach, Charles A. ..... St. Paul
‡ Roach, Donald E. ..... St. Paul
‡ Rolig, David H. ..... West St. Paul
Romero, Jose B. ..... St. Paul
†‡ Rosenthal, Robert ..... St. Paul
‡ Roth, George C. ..... St. Paul
Rowe, Clarence J., Jr. ..... St. Paul
‡ Roy, Philemon C. ..... St. Paul
† Ruhberg, George N. ..... Santa Barbara, CA
‡ Rukavina, John G. ..... St. Paul
‡ Rushay, Arthur J. ..... White Bear Lake
‡ Rusterholz, Alan P. ..... St. Paul
†‡ Ryan, John J. ..... St. Paul
‡ Ryan, Joseph M. ..... St. Paul
‡ Sand, Richard E. ..... St. Paul
‡ Sargent, John H. ..... St. Paul
‡ Savett, Laurence A. ..... St. Paul
Saxena, Krishna M. ..... St. Paul
‡ Schaffhausen, George E. ..... St. Paul
‡ Scherek, Jerome J. ..... St. Paul
‡ Schloff, Ivan ..... St. Paul
Schloff, Leonard D. ..... St. Paul
Schmidtke, Reinhardt L. ..... Minneapolis
‡ Schochet, H. Laurence ..... St. Paul
† Schons, Edward ..... Minnetonka Beach
‡ Schossow, George W. ..... White Bear Lake
‡ Schroeckenstein, Hugo F. ..... St. Paul
‡ Schultz, Paul E. ..... St. Paul
Schwartzkopff, Othild ..... St. Paul
‡ Scott, Eugene E. ..... St. Paul
£ Sejvar, Joseph P. ..... St. Paul
Sekhon, Mohan S. ..... St. Paul
‡ Sells, Richard J. ..... St. Paul
‡ Sethre, Arthur E. ..... St. Paul
†‡ Setzer, Hobert J. ..... St. Paul
† Shannon, William R. ..... Faribault
Shear, Howard H. ..... West St. Paul
‡ Shelander, Marcus I. ..... St. Paul
Siegel, Clarence ..... St. Paul
‡ Siegel, Leighton G. ..... St. Paul
Simmonds, Harry N. L. ..... St. Paul

Ramsey County Medical Society *(Continued)*

‡ Simons, Leander T. ..... St. Paul
‡ Singer, Benjamin J. ..... St. Paul
‡ Skinner, Abbott ..... St. Paul
† Skinner, Harvey O. ..... St. Paul
‡ Smiley, Donald P. ..... St. Paul
†‡ Smisek, Elmer A. ..... St. Paul
‡ Smith, H. Nippert ..... St. Paul
£ Smith, James C. ..... St. Paul
Smith, Vernon D. E. ..... St. Paul
‡ Smith, William T. ..... St. Paul
† Snyder, George W. ..... St. Paul
†‡ Sohlberg, Olof I. ..... St. Paul
‡ Sommerdorf, Vernon L. ..... St. Paul
Sorem, Milton B. ..... St. Paul
Soucheray, Philip H. ..... St. Paul
†‡ Souster, Benjamin B. ..... St. Paul
Sowada, Ernest J. ..... St. Paul
‡ Sperl, Michael P., Jr. ..... St. Paul
Sprafka, Gregory A. ..... St. Paul
‡ Sprafka, Joseph L. ..... St. Paul
‡ Spraitz, Anton F., Jr. ..... St. Paul
‡ Stafne, John G. ..... St. Paul
‡ Steinberg, Charles L. ..... St. Paul
‡ Sterner, Donald C. ..... St. Paul
*‡ Sterner, Ernest R. ..... St. Paul
‡ Sterner, John J. ..... St. Paul
Straus, Maurice L. ..... St. Paul
‡ Strem, Edward L. ..... St. Paul
‡ Sturley, Rodney F. ..... St. Paul
‡ Sullivan, W. Albert, Jr. ..... St. Paul
‡ Swanson, Lawrence J. ..... West St. Paul
‡ Swanson, Ralph H. ..... West St. Paul
† Swendson, James J. ..... St. Paul
‡ Swenson, Donald B. ..... St. Paul
‡ Taddeini, Luigi ..... St. Paul
‡ Tanasichuk, Murray A. ..... St. Paul
‡ Tani, George ..... St. Paul
‡ Tate, Wayne E. ..... South St. Paul
‡ Teeter, Richard R. ..... St. Paul
‡ Teisberg, John E. ..... St. Paul
‡ Thalhuber, Wayne H. ..... St. Paul
‡ Thompson, Wayne W. ..... St. Paul
Tiffany, Francis B. ..... St. Paul
‡ Tifft, Cyril R. ..... St. Paul
‡ Tongen, Lyle A. ..... St. Paul
‡ Travis, James S. ..... St. Paul
Tregilgas, Richard B. ..... St. Paul
‡ Trotman, Neil M. ..... St. Paul
‡ Troup, Elliott ..... St. Paul
Trow, William H. ..... St. Paul
Tveten, Omar A. ..... St. Paul
‡ Ubel, Frank A. ..... St. Paul
Vaccarella, R. James ..... St. Paul
* Vail, David J. ..... St. Paul
‡ Van Bergen, Frederick H. ..... Minneapolis
‡ Van De Riet, Lowell W. ..... St. Paul
Varco, Richard L. ..... St. Paul
‡ Vaughn, C. Gordon ..... St. Paul
Veinbergs, Arnold ..... St. Paul
† Veirs, Dean M. ..... Hastings
† Venables, Alexander E. ..... Marysville, WV
‡ Venters, Homer D., Jr. ..... St. Paul
‡ Votel, Thomas W. ..... St. Paul
‡ Waas, Charles W. ..... St. Paul
† Walker, Arthur E. ..... St. Paul
‡ Wall, James O. ..... St. Paul
‡ Walsh, Edward F. ..... St. Paul
‡ Walsh, William E. ..... St. Paul
‡ Walter, Clarence W. ..... St. Paul
Wangsness, Mary S. ..... St. Paul
Warhol, Richard M. ..... St. Paul
‡ Warner, Clyde M. ..... St. Paul
‡ Warren, Cecil A. ..... St. Paul
Waters, Alvin W. ..... St. Paul
‡ Watson, P. Theodore ..... St. Paul
‡ Watson, William H. A. ..... St. Paul
‡ Watson, William J. ..... Newport
Watz, Clarence E. ..... St. Paul
Webb, Alex G., Jr. ..... St. Paul
Webber, Fred L. ..... St. Paul
‡ Wedes, Deno J. ..... St. Paul
‡ Weier, Thomas E. ..... St. Paul
Weigant, Charles E. ..... Fort Snelling
‡ Weis, Benjamin A. ..... St. Paul
† Weisberg, Maurice ..... St. Paul
‡ Wenzel, Gilbert P. ..... St. Paul
£ Westermeyer, Joseph J. ..... St. Paul
‡ Westover, Darrell E. ..... St. Paul
Wetteland, Thomas F. ..... West St. Paul
Wetzel, Earl V. ..... St. Paul
Whiting, F. Douglas ..... St. Paul
Wiencke, William M. ..... St. Paul
‡ Wier, G. Thomas ..... St. Paul
‡ Williams, George E. ..... St. Paul
‡ Williams, Harry J., III ..... St. Paul
‡ Williams, Hugh J. ..... St. Paul
‡ Williams, John A. ..... St. Paul
Williams, Richard A. ..... Cottage Grove
‡ Wilson, Fred B. ..... St. Paul
‡ Winter, Robert B. ..... St. Paul
Wolkoff, Hyman J. ..... St. Paul
‡ Woodburn, Robert L. ..... St. Paul
‡ Woolfrey, Bertram F. ..... St. Paul
YaDeau, Richard E. ..... St. Paul
Youngren, Everett R. ..... St. Paul
‡ Zachman, Leo L. ..... St. Paul
‡ Zagaria, James F. ..... St. Paul
‡ Zarling, Max E. ..... St. Paul

RANGE MEDICAL SOCIETY

Koochiching, Itasca and the Northern Portion of
St. Louis County
Regular meetings, fourth Tuesday of the Month
Annual meeting, January
Number of members 119

PRESIDENT
Crow, George M. ..... Hibbing
SECRETARY
Eisenman, Walter ..... Hibbing
CORRESPONDING SECRETARY
Evans, Mrs. Virginia ..... Hibbing

Ahola, Kenneth E. ..... Hibbing
Alexander, Paul J. ..... Hibbing
Anderson, Russell H. ..... Virginia
Antonelli, Jordan J. ..... Hibbing
Antonow, Arthur M. ..... Virginia
Arko, Frank R. ..... Hibbing
Avren, Barbara L. ..... Virginia
Baich, Velemir M. ..... Coleraine
Balderson, Robert P. ..... Grand Rapids
Baraga, Anthony R. ..... Hibbing
Barnes, Richard E. ..... Aurora
Bartholdt, H. Peter ..... Cook
*† Benell, Otto E. ..... Britt
Bernal, Jorge ..... Virginia
Bolz, J. Arnold ..... Grand Rapids
Bonner, John L. ..... Grand Rapids
Braun, Ohrmundt C. ..... Grand Rapids
£ Brende, Joel O. ..... Topeka, KS
Campos, Amador ..... Aurora
Chermak, Francis G. ..... Phoenix, AZ
‡ Ciriacy, Edward W. ..... Minneapolis
Coe, Robert O. ..... Virginia
Cope, Hershel B. ..... Virginia
Coy, Douglas J. ..... Grand Rapids
Crow, George M. ..... International Falls
Davenport, Jay A. ..... Virginia
DeMarais, Lloyd C. ..... Hibbing
Decker, Charles W. ..... Hibbing
Dobler, Manfred G. ..... Ely
Drucker, Franklin G. ..... Bigfork
Eisenman, Walter ..... Hibbing
‡ Engelstad, Wendell P. ..... Virginia
Erickson, Vernon D. ..... Grand Rapids
Evensta, John B. ..... Grand Rapids
Ewens, George B. ..... Virginia
Flynn, Bernard F. ..... Hibbing
French, Bayard T. ..... Hibbing
Friedlieb, Oskar P. ..... Virginia
Gerend, Thomas J. ..... Virgina
Glomstad, Gary B. ..... Grand Rapids
Goodall, David C. ..... Deer River
Gorden, A. Marc ..... International Falls
Grahek. Jack P. ..... Ely
Greene, Gordon O. ..... Hibbing
Grinley, Andrew V. ..... Grand Rapids
Halper, Bernard ..... Hibbing
Halverson, Kermit J. ..... Parkville
* Hanover, Ralph D. ..... International Falls
Hansen, Robert E. ..... Hibbing
† Heiam, William C. ..... Cook
Helwig, Karl L. ..... Virginia
Holm, Owen W. ..... Hibbing
Iammatteo, Pat ..... Hibbing
Ibrahim, George W. ..... Virginia
Iverson, Paul C. ..... Grand Rapids
† Jacobson, Clarence ..... Chisholm
Johnson, Calvin J. ..... Grand Rapids
Johnsrud, Luverne ..... Hibbing
Johnston, H. Wayne ..... Virginia
Karges, Laurel E. ..... Grand Rapids
Karish, Louis J. ..... Grand Rapids
‡ Kelly, Robert T. ..... Grand Rapids
Kiesler, Frank ..... Grand Rapids
† Kotchevar, Frank R. ..... Sun City, CA
Kruger, E. Larry ..... Nashwauk
Law, Harrison E. ..... Virginia
Leach, Thomas C. ..... Babbitt
Lee, William C. ..... Hibbing
Leih, George G. ..... Virginia
Leino, Walter B. ..... Ely
McClelland, John G. ..... Virginia
McKenna, John J. ..... Virginia
McKenna, Maurice J. ..... Grand Rapids
Martinson, Raymond M. ..... Virginia
Mast, Fredric L. ..... Chisholm
Miettunen, John B. ..... Hibbing
Miks, George M. ..... Aurora
Miller, Harry G. ..... Virginia
Mock, Charles J. ..... Virginia
Moyer, Richard R. ..... Hibbing
Mueller, Donald R. ..... Grand Rapids
Muller, John J. ..... Hibbing
Murray, Robert A. ..... Hibbing
Neff, Walter S. ..... Britt
Nelimark, Donald R. ..... Virginia
Nelson, Bernette G. ..... Ely
‡ Nollet, Donald J. ..... Hibbing
Olson, Richard T. ..... Virginia
Owens, Ben P. ..... Hibbing
Paciotti, Vincent J. ..... Hibbing
Parker, Wilbert H. ..... Chisholm
Payne, Richard E. ..... Virginia
Person, Duane F. ..... Virginia
Peterson, Edward N. ..... Virginia
Pietan, Jerald H. ..... Chisholm
Prlina, Isaac M. ..... Virginia
Rayer, Anthony L. ..... Babbitt
Reed, Paul ..... Virginia
Reynolds, Dermot F. ..... Hibbing
Richter, David J. ..... Virginia
Roth, Albert H. ..... Deer River
† Rowles, Everett K. ..... Laguna Hills, CA
†‡ Salter, Reginald A. ..... Virginia
Schirber, Martin J. ..... Grand Rapids
Schweiger, Theodore R. ..... Hibbing
Schwinghamer, Thomas G. ..... Ely
Sher, David A. ..... Virginia
Siegel, John S. ..... Virginia
† Sisler, Clifford E. ..... Grand Rapids
† Snyker, Omer E. ..... Ely
Stolen, Keith H. ..... Grand Rapids
Strouth, Jonas C. ..... Virginia
Summar, M. Thomas ..... Virginia
Swenson, Floyd J. ..... Grand Rapids
Talsness, Jon M. ..... International Falls
Tietz, Charles A. ..... Virginia
‡ Walker, Stuart B. ..... Aurora
‡ Walter, Frederick H. ..... International Falls
Weir, Mathew J. ..... Virginia
‡ Werner, Donald L. ..... Hoyt Lakes
Wheeler, Gilbert S. ..... Virginia
‡ Woodruff, Whitney ..... Virginia

RED RIVER VALLEY MEDICAL SOCIETY

Kittson, Mahnomen, Marshall, Norman, Pennington,
Polk, Red Lake and Roseau Counties
Regular meetings, quarterly
Annual meeting, December
Number of members 49

PRESIDENT
Sather, George A. ..... Fosston

SECRETARY
Dillenburg, Cyril ..... Crookston

Behr, Orlo K. ..... Crookston
‡ Berg, Arnold M. ..... Thief River Falls
† Bratrud, Edward ..... Alexandria
Bray, Jerome L. ..... Thief River Falls
Brown, Glenn W. ..... Halstad
Brown, James R. ..... Crookston
Carter, Robert G. ..... Thief River Falls
Choithani, C. M. ..... Crookston
Clapp, Hubert D. ..... Crookston
Dagg, Earl ..... Thief River Falls
Davidson, Duane J. ..... Thief River Falls
Dillenburg, Cyril ..... Crookston
† Flancher, Leon H. ..... Detroit Lakes
† Foderick, Peter P. ..... Ada
Herber, Leo ..... Thief River Falls
Hirsh, Stanton ..... Crookston
Holmstrom, Carle H. ..... Warren
Kinkade, Byron R. ..... Ada
‡ Klefstad, Lloyd H. ..... Greenbush
† Kostick, William R. ..... Fertile
Larter, Roland R. ..... Hallock
† Loken, Theodore ..... Ada
† Lynde, Orrin G. ..... Los Gatos, CA
Martin, George B. ..... Thief River Falls
Mercil, William ..... Crookston
Mersy, David J. ..... Red Lake Falls
Montaniel, Necito L. ..... Crookston
† Nelson, Henry E. ..... Crookston
† Oppegaard, C. L. ..... Scottsdale, AZ
Parra, Samuel ..... Crookston
Pinsonneault, W. A. ..... Roseau
Pollman, Stanley E. ..... Naha, Okinawa
Pumala, Erven E. ..... Warren
† Roholt, Christian L. ..... McIntosh
Reff, Alan R. ..... Crookston
Sather, Edgar L. ..... Fosston
Sather, George A. ..... Fosston
‡ Sather, Richard N. ..... Fosston
Sather, Russell O. ..... Crookston
Scheuneman, Allen F. ..... Thief River Falls
Schnabel, Norma B. ..... Crookston
Schnabel, Robert F. ..... Crookston
Skogerboe, Rudolph ..... E. Grand Forks
Stadem, Clifford ..... Crookston
Stewart, Donald E. ..... Crookston
Taylor, Ross M. ..... Thief River Falls
Thorbus, Ruben S. ..... Karlstad
Thorsgard, Ernest O. ..... Thief River Falls
Uhley, Charles G. ..... Hopkins
Wendt, Paul ..... Thief River Falls
Wikoff, Howard M. ..... Crookston

RICE COUNTY MEDICAL SOCIETY

Rice County
Regular meetings, third Tuesday of
January, April, September and November
Annual meeting in November
Number of members 30

PRESIDENT
Tuma, Ben ..... Faribault

SECRETARY
Clarke, Dean T. ..... Faribault

Beaton, J. Gordon ..... Northfield
Bruhl, Heinz H. ..... Faribault
Buesgens, Ralph H. ..... Waterville
Clarke, Dean ..... Faribault
*† Engberg, Edward J. ..... Faribault
Faust, John H. ..... Northfield
Foni, Iancu F. ..... Faribault
†‡ Francis, David W. ..... Morristown
Good, Roy H. ..... Northfield
Graham, Asa B. ..... Faribault
Gutzmann, Bruce F. ..... Faribault
Haas, Jack F. ..... Northfield
Halvorson, David C. ..... Northfield
£ Hanson, Mark T. ..... Faribault
† Kennedy, George L. ..... Faribault
† Kolars, James J. ..... Faribault
Meyer, Frederick C. ..... Kenyon
† Meyer, Paul F. ..... Faribault
Meyer, Richard H. ..... Faribault
Meyer, Robert P. ..... Faribault
Nickerson, John R. ..... Faribault
Orr, Burton A. ..... Faribault
† Rumpf, Carl W. ..... Faribault
Rysgaard, George N. ..... Northfield
Smith, Thorsten ..... Theills, NY
Speckhals, Robert C. ..... Faribault
Street, Bernard ..... Northfield
Studer, Donald J. ..... Faribault
† Traeger, Carl A. ..... Faribault
Tuma, Ben ..... Faribault
Watts, George W. ..... Ithaca, NY
Weaver, Paul H. ..... Faribault

ST. LOUIS COUNTY MEDICAL SOCIETY

Carlton, Cook, Lake and Southern portion of
St. Louis County
Regular meetings, second Thursday in each month
except July and August
Annual meeting, second Thursday in January
Number of members 206

PRESIDENT
Asta, Joseph J. ..... Duluth
SECRETARY
Thurn, Roy J. ..... Duluth
SECRETARY, EXECUTIVE OFFICE
Lundgren, Miss Margaret M. ..... Duluth
‡ Abraham, Arden L. ..... Duluth
‡ Ahrens, Curtis F. ..... Duluth
‡ Anderson, James M. ..... Duluth
Armin, David W. ..... Two Harbors
‡ Asta, Joseph J. ..... Duluth
† Athens, A. G. ..... Santa Barbara, CA
‡ Atmore, William G. ..... Duluth
‡ Aufderheide, Arthur C. ..... Duluth
Backus, Byron C. ..... Cloquet
‡ Backus, Lloyd B. ..... Cloquet
† Backus, Reno W. ..... Cloquet
‡ Bagley, Charles M. ..... Duluth
Bagley, Elizabeth C. ..... Duluth
‡ Bakkila, Henry E. ..... Duluth
‡ Balmer, Albert I. ..... Duluth
‡ Bartzen, Peter J. ..... Duluth
‡ Becker, Frederic T. ..... Duluth
‡ Bell, Harry M., Jr. ..... Duluth
† Bepko, Marie (Puumala) ..... Cloquet
‡ Bergan, Robert O. ..... Duluth
‡ Berns, Max H. ..... Duluth
†‡ Bianco, Anthony J. ..... Duluth
† Bloom, Joseph ..... Pompano Beach, FL
Blum, Clifford J. ..... Duluth
‡ Boecker, Bernhard ..... Duluth
† Boman, Paul G. ..... Duluth
‡ Boman, Peter L. ..... Duluth
‡ Boyer, Samuel H. ..... Duluth
‡ Bray, Philip N. ..... Duluth
‡ Brooker, Warren J. ..... Duluth
‡ Brown, Cyrus C., Jr. ..... Duluth
‡ Buckley, Robert P. ..... Duluth
‡ Bulluck, Matthew H. ..... Duluth
‡ Butler, John K. ..... Cloquet
‡ Campaigne, Robert J. ..... Duluth
‡ Carter, Robert E. ..... Duluth
‡ Christensen, Clarence H. ..... Duluth
Church, Gerald E. ..... Two Harbors
Clark, Elizabeth A. (Mrs. Halbert) ..... Duluth
‡ Clark, Ivan T. ..... Sun City, AZ
Clifford, Thomas M. ..... Silver Bay
‡ Coll, James J. ..... Duluth
‡ Collins, Roger T. ..... Duluth
‡ Cotton, Gerald E. ..... Duluth
‡ Coventry, William D. ..... Duluth
‡ Cowan, Gary A. ..... Duluth
‡ Cowan, George M. ..... Duluth
Cox, Milton J. ..... Duluth
‡ Creps, James R. ..... Duluth
‡ Davidson, A. Dale ..... Duluth
Davis, William ..... Moose Lake
‡ Deutsch, Robert J. ..... Duluth
†‡ Dickson, Franklin H. ..... Proctor
‡ Dobbs, Richard L. ..... Duluth
‡ Drexler, Charles J. ..... Duluth
‡ Dwyer, John J. ..... Duluth
£ Eckman, Matthew J. ..... Minneapolis
‡ Eckman, Philip F. ..... Duluth
‡ Eckman, Philip L. ..... Duluth
‡ Eckman, Ralph J. ..... Duluth
‡ Ecklund, Carl D. ..... Duluth
‡ Emanuel, Karl W. ..... Duluth
‡ Engelsgjerd, Gerald L. ..... Duluth
Evison, Emerson O. ..... Duluth
‡ Fawcett, Keith R. ..... Duluth
*‡ Fellows, Manley F. ..... Duluth
Feuling, John C. ..... Sun City, AZ
‡ Fifield, Malcolm M. ..... Duluth
‡ Fisketti, Henry ..... Duluth
Frederickson, David L. ..... Duluth
‡ Fuller, Josiah ..... Duluth
†‡ Gillespie, Malcolm G. ..... Duluth
‡ Goldish, Daniel R. ..... Duluth
‡ Goldish, Robert J. ..... Duluth
‡ Goldschmidt, Volker ..... Duluth
‡ Goodnow, William H. ..... Duluth
‡ Gowan, Lawrence R. ..... Duluth
‡ Gowan, Lawrence R., Jr. ..... Duluth
‡ Grohs, William H. ..... Duluth
‡ Gower, Walter E. ..... Duluth
Gronquist, Y. K. J. ..... Cloquet
Haase, Donald D. ..... Silver Bay
‡ Haavik, John E. ..... Duluth
Halbert, John J. ..... Duluth
‡ Halliday, Phillip V. ..... Duluth
Hanson, Ernest O. ..... Cloquet
Harper, David G. ..... Duluth
‡ Harrington, Vernon A. ..... Duluth
Hartzell, Allan ..... Duluth
‡ Heisel, John G. ..... Duluth
Henry, Harold W. ..... Moose Lake
‡ Hilding, Anderson C. ..... Duluth
Hoeg, Dwight C. ..... Duluth
‡ Hoff, Herbert O. ..... Duluth
‡ Holt, Glen E. ..... Duluth
‡ Hood, Roderick P. ..... Duluth
Houglum, Arvid J. ..... Duluth
†‡ Houkom, S. Sverre ..... Duluth
† Hutchinson, Henry ..... Brainerd
Jacklin, Alexander J. ..... Duluth
‡ Jacobson, Ferdinand C. ..... Duluth
‡ Jacott, William E. ..... Duluth
‡ Jeronimus, Henry J. ..... Duluth
* Jessico, Charles M. ..... Duluth
‡ Johnson, Franklin L. ..... Duluth
‡ Johnson, Karl E. ..... Duluth
‡ Johnson, Theodore L. ..... Duluth
‡ Juntunen, Roy R. ..... Duluth
‡ Kilen, Mark B. ..... Duluth
†‡ Klein, Harry ..... Duluth
‡ Knoedler, John P. ..... Duluth
Kosiak, William ..... St. Paul
Kubista, Theodore P. ..... Duluth
‡ Kundel, Donald W. ..... Duluth
‡ Kwako, Jerome E. ..... Duluth

St. Louis County Medical Society *(Continued)*

‡ L'Abbe, A. J. Philip ..... Duluth
‡ LaBree, Robert H. ..... Duluth
‡ Langseth, Rodney N. ..... Duluth
‡ Larson, Donald M. ..... Duluth
Larson, Kenneth R. ..... Moose Lake
‡ Latterell, Kenneth E. ..... Duluth
‡ Leek, Joseph H. ..... Duluth
Leonardson, Peter Y. ..... Silver Bay
Leppink, Harold B. ..... Two Harbors
Leppo, N. Erkki A. ..... Duluth
‡ Linnell, Leonard S. ..... Duluth
†‡ Litman, Samuel N. ..... Duluth
†‡ McNutt, John R. ..... Duluth
MacDonald, Roger A. ..... Grand Marais
†‡ MacRae, Gordon C. ..... Duluth
† Magney, Fredolph H. ..... Duluth
Martin, Webster C. ..... Duluth
‡ Maryland, Daniel L. ..... Duluth
Mathers, John E. ..... Duluth
‡ Mattson, Roger A. ..... Duluth
‡ May, Horst G. ..... Duluth
‡ Mendesh, Anthony N. ..... Duluth
‡ Merrick, William G. ..... Duluth
‡ Meyer, Howard J. ..... Duluth
Michaelis, Dorothy ..... Duluth
Moller, Julie C. ..... Duluth
Monge', James J. ..... Duluth
‡ Monserud, Nels O. ..... Cloquet
‡ Moyer, John B. ..... Duluth
Munger, James E. ..... Duluth
Munson, Martin S. ..... Moose Lake
‡ Myers, Thomas T., III ..... Duluth
Nelson, John W. ..... Duluth
‡ Nisius, George F. ..... Duluth
‡ Nisswandt, Albert L. ..... Duluth
† Norberg, Carl E. ..... Los Altos, CA
‡ O'Neill, John C. ..... Duluth
‡ Parson, E. Irvine ..... Duluth
‡ Pasek, Antone W. ..... Cloquet
Patch, Orien B. ..... Duluth
‡ Peterson, John H. ..... Duluth
Pollard, William S. ..... Duluth
‡ Power, John E. ..... Duluth
Puumala, Barbara M. ..... Cloquet
Puumala, Reino H. ..... Cloquet
Puumala, Ricard R. ..... Cloquet
‡ Reardon, Andrew E. ..... Duluth
‡ Reed, Henry H. ..... Duluth
‡ Rowe, Richard G. ..... Duluth
‡ Rudie, Peter S. ..... Duluth
‡ Rudie, William D. ..... Duluth
‡ Runquist, John M. ..... Duluth
‡ Ruth, Bradley R. ..... Duluth
‡ Ryan, Edward A. ..... Duluth
* Sach-Rowitz, Alvan ..... Moose Lake
Saloum, Lucille M. ..... Duluth
* Sandell, Samuel T. ..... Duluth
Sanford, John B. ..... Duluth
Sax, Milton H. ..... Duluth
* Sax, Simon G. ..... Duluth
‡ Schmid, John F. ..... Duluth
† Schneider, Lawrence E. ..... Duluth
‡ Shirley, Raymond M. ..... Duluth
Slack, William J. ..... Duluth
‡ Smith, Cyril M. ..... Duluth
Smith, Wallace R. ..... Grand Marais
† Spang, Anthony J. ..... Duluth
†‡ Spang, James S. ..... Duluth
‡ Spang, William M. ..... Duluth
‡ Spencer, Joseph F. ..... Duluth
‡ Stein, William A. ..... Duluth
Stolee, Thomas A. ..... Duluth
‡ Storsteen, Kenneth A. ..... Duluth
‡ Streitz, John M. ..... Duluth
‡ Strewler, Gordon J. ..... Duluth
‡ Swedberg, William A. ..... Duluth
‡ Swensen, Don P. ..... Duluth
†‡ Swenson, Arnold O. ..... Duluth
Swenson, Orville P. ..... Cloquet
Teich, Kenneth W. ..... McKeesport, PA
Terrell, Bernard J. ..... Nopeming
‡ Tetlie, James P. ..... Duluth
‡ Thomas, John V. ..... Duluth
‡ Thompson, James I. ..... Duluth
‡ Thurn, Roy J. ..... Duluth
‡ Tosseland, Noel E. ..... Duluth
‡ Tygart, Robert L. ..... Duluth
‡ Ulrich, Emery E. ..... Duluth
Van Druten, William A. ..... Duluth
‡ Van Puffelen, Paul S. ..... Duluth
Van Ryzin, Donald J. ..... Duluth
‡ Wahman, Robert E. ..... Duluth
‡ Walder, Harold J. ..... Duluth
‡ Wall, Jack E. ..... Duluth
‡ Wallace, Martin O. ..... Duluth
†‡ Wells, Arthur H. ..... Duluth
‡ Williams, Bruce F. P. ..... Duluth
‡ Wolfe, John W. ..... Duluth
‡ Young, Hadley R. ..... Duluth

SCOTT-CARVER COUNTY MEDICAL SOCIETY

Scott and Carver Counties
Regular meetings, first Wednesday of each month,
except July and August
Annual meeting in June
Number of members 45

PRESIDENT
Kuz, Eugene L. ..... Savage

SECRETARY
Crislip, George D. ..... Waconia

Abrams, Donald J. ..... Shakopee
Adams, Patrick J. ..... Shakopee
Amra, Waleed ..... Chaska
Bean, Charles N. ..... Waconia
Berg, John H. ..... Montgomery
‡ Bratholdt, James W. ..... Watertown
† Buck, Frederick H. ..... Shakopee
‡ Cervenka, Charles F. ..... New Prague
Cervenka, John D. ..... New Prague
Clarke, John W. ..... Waconia
Cowger, Robert C. ..... Farmington
‡ Crislip, George D. ..... Waconia
‡ Doherty, Elmer M. ..... New Prague
Erickson, Robert L. ..... Rosemount
Hallgren, Roger ..... Belle Plaine
Heagle, C. Russell ..... Waconia
† Hebeisen, Milton B. ..... Chaska
Heinz, Ivy ..... Shakopee
‡ Heinzerling, Carl R. ..... Chaska
†‡ Juergens, Herman M. ..... Belle Plaine
KLC-Mikusciak, George M. ..... Belle Plaine
† Kucera, Stanley T. ..... Northfield
‡ Kuz, Eugene ..... Savage
Larson, Leighton W. ..... Waconia
Lehmann, James D. ..... Waconia
Lin, Hong-Chien ..... Waconia
‡ Lukk, Olaf ..... Prior Lake
† McDaniel, Samuel P. ..... Lakeville
Mendiola, Ramon P., Jr. ..... Waconia
‡ Nehring, John ..... Chaska
‡ Olson, Richard E. ..... Chaska
Palattao, Augustin D., Jr. ..... Waconia
‡ Pearson, Bror F. ..... Shakopee
‡ Philip, David R. ..... Watertown
‡ Pistulka, Rolland D. ..... Chaska
Ponterio, James E. ..... Shakopee
Provence, Cecil L. ..... Waconia
Rieschl, Elizabeth K. ..... Jordan
Rynda, Edwin R. ..... New Prague
‡ Schimelpfenig, George T. ..... Chaska
Spagnolo, Anthony A. ..... Shakopee
Stahler, Paul A. ..... Jordan
Wempner, Jon D. ..... Waconia
†‡ Westerman, Alvin E. ..... Montgomery
†‡ Westerman, Fred C. ..... Montgomery

SIBLEY COUNTY MEDICAL SOCIETY

Sibley County
Regular meetings, 3rd Monday of Odd number months
Annual meeting in November
Number of members 5

PRESIDENT
Vener, John M. ..... Arlington

SECRETARY
Knoche, Harvey A. ..... Gaylord

Bergersen, Dean ..... Arlington
Dysterheft, Adolph ..... Gaylord
† Kath, Reinhard H. ..... Merrifield
Knoche, Harvey A. ..... Gaylord
Vener, John M. ..... Arlington

SOUTHWESTERN MINNESOTA MEDICAL SOCIETY

Cottonwood, Jackson, Murray, Nobles, Pipestone and
Rock Counties
Regular meetings first Monday of each month
except June, July and August
Annual meeting, November
Number of members 52

PRESIDENT
Heiberg, O. M. ..... Worthington

SECRETARY
Boone, Ervin S. ..... Luverne
‡ Bader, Jean L. ..... Slayton
‡ Basinger, Harold P. ..... Windom
† Basinger, Homer P. ..... Windom
‡ Beckering, Gerrit ..... Edgerton
‡ Beckering, Roland G. ..... Edgerton
† Benjamin, Walter G. ..... Pipestone
† Bofenkamp, Ferdinand W. ..... Luverne
‡ Boone, Ervin S. ..... Luverne
‡ Boyd, Frank E. ..... Pipestone
‡ Carlson, John V. ..... Westbrook
‡ Carlson, Lloyd E. ..... Worthington
‡ Christiansen, Harold A. ..... Jackson
‡ Dawson, Lorin D. ..... Worthington
‡ Dokken, James H. ..... Windom
‡ Doman, Victor W. ..... Lakefield
‡ Eaton, David B. ..... Worthington
‡ Faul, Bennie C. ..... Worthington
‡ Fitch, Charles G. ..... Worthington
‡ Glick, Dallas D. ..... Mountain Lake
‡ Hallin, Roger P. ..... Worthington
†‡ Halloran, Walter H. ..... Jackson
‡ Halpern, David J. ..... Brewster
‡ Harrison, Percy W. ..... Worthington
‡ Hegstad, Thomas C. ..... Windom
‡ Heiberg, O. M. ..... Worthington

Southwestern Minnesota Medical Society *(Continued)*

‡ Keyes, Robert W. ..... Pipestone
†‡ Kilbride, Edwin A. ..... Worthington
‡ Kim, Kyoung ..... Worthington
‡ Kotval, Russell J. ..... Pipestone
‡ Laikola, Leslie A. ..... Adrian
£ Larsen, Russell H. ..... Burnsville
‡ Lohmann, John G. ..... Pipestone
‡ Minge, Raymond K. ..... Worthington
‡ Mork, John N. ..... Worthington
‡ Nealy, Donald E. ..... Adrian
‡ Nywall, Dean D. ..... Slayton
‡ Odland, Donald M. ..... Luverne
‡ Patterson, Hugh D. ..... Slayton
‡ Pierce, Robert B. ..... Heron Lake
‡ Pierson, Roy F. ..... Slayton
‡ Plucker, Milton W. ..... Worthington
‡ Rud, Paul D. ..... Luverne
Ryding, Vincent ..... Ames, IA
† Schade, Frederick ..... Santa Cruz, CA
‡ Seisler, Edward P. ..... Worthington
‡ Siebert, Darrel W. ..... Luverne
‡ Stam, John ..... Worthington
‡ Strand, Jack W. ..... Jasper
† Stratte, Harold C. ..... Windom
‡ Strough, LaVern C. ..... Worthington
‡ Wells, Walter B. ..... Jackson
‡ Wiens, Alvin L. ..... Mountain Lake
† Williams, Charles A. ..... Seattle, WA

STEARNS-BENTON COUNTY MEDICAL SOCIETY

Stearns and Benton Counties
Regular meetings, third Thursday of each month
Annual meeting, January
Number of members 102

PRESIDENT
Sommers, Stephen D. ..... St. Cloud
SECRETARY
Espelien, Alan D. ..... St. Cloud
SECRETARY, EXECUTIVE OFFICE
Anderson, Mrs. Joyce E. ..... St. Cloud
‡ Alden, Charles W. ..... Sauk Rapids
Aulick, Ernest J. ..... Paynesville
‡ Autrey, William A. ..... St. Cloud
Ballantine, Jerome J. ..... St. Cloud
‡ Bancroft, Burton R., Jr. ..... St. Cloud
Bauman, John C. ..... Foley
Baumgartner, Florian H. ..... Albany
Belshe, Joseph ..... St. Cloud
‡ Berger, Phil R. ..... St. Cloud
‡ Beuning, John B. ..... St. Cloud
‡ Bozanich, Milosh S. ..... St. Cloud
‡ Brattensborg, Henry J. ..... St. Cloud
‡ Brigham, Charles F., Jr. ..... St. Cloud
‡ Broker, Henry M. ..... St. Cloud
‡ Brown, Frank T. ..... St. Cloud
‡ Cesnik, Robert J. ..... Sauk Rapids
‡† Clark, Harry B. ..... St. Cloud
Courteau, Robert D. ..... Rodesia, Africa
Cress, Thomas L. ..... St. Cloud
‡ Cumming, Robert J. ..... St. Cloud
Dahlquist, LaRue V. ..... St. Cloud
†‡ Donaldson, Charles S. ..... St. Cloud
Dubois, Julian F. ..... Sauk Centre
‡ Dziubinski, Emil H. ..... St. Cloud
Espeland, L. Michael ..... Bellevue, NB
‡ Espelien, Alan D. ..... St. Cloud
‡ Evans, Leslie M. ..... Sauk Rapids
‡ Gaida, Joseph B. ..... St. Cloud
Gerstenkorn, George B. ..... Milaca
Goehrs, Gilman H. ..... St. Cloud
Gonzales, Neva M. ..... St. Cloud
Grant, John C. ..... Sauk Centre
† Halenbeck, Philip L. ..... St. Cloud
‡ Harbaugh, John T. ..... St. Cloud
‡ Held, William J. ..... St. Cloud
† Henry, Clarence J. ..... Onamia
Henry, Joseph E. ..... Milaca
Hobday, H. Thomas ..... St. Cloud
‡ Hughes, Bernard J. ..... St. Cloud
† Hutchinson, Henry ..... Brainerd
Iverson, Jerry A. ..... St. Cloud
‡ Jaeger, Dwight E. ..... St. Cloud
‡ John, Byron L. ..... St. Cloud
‡ Johnson, William E. ..... St. Cloud
†‡ Jones, Richard N. ..... St. Cloud
Keith, Paul J. ..... Milaca
‡ Kelly, James H. ..... St. Cloud
‡ Kelly, John F. ..... Cold Spring
‡ Koenig, Robert P. ..... St. Cloud
‡ Kruzich, Stephen J. ..... St. Cloud
Kuhlmann, Lawrence B. ..... Melrose
‡ Kvistberg, Gerald K. ..... St. Cloud
LaFond, Edward M. ..... St. Cloud
‡ Lenarz, Albert J. ..... St. Cloud
Lindeman, Raymond J. ..... Paynesville
‡ Loeb, George L. ..... St. Cloud
‡ Loes, Louis, A. ..... St. Cloud
‡ Luby, Thomas H. ..... St. Cloud
Lyons, John R. ..... St. Cloud
† McDowell, John P. ..... St. Cloud
McNamara, John P. ..... Rice
‡ May, Robert B. ..... St. Cloud
† Milhaupt, Emmett N. ..... Dunedin, FL
‡ Moran, Paul T. ..... St. Cloud
Mueller, Rudolph B. ..... Richmond
‡ Murn, Thomas G. ..... St. Cloud
‡ Murray, Robert A., Jr. ..... St. Cloud
* Musachio, Nicholas F. ..... St. Paul
† Myre, Clifford R. ..... Paynesville
Neils, Vernon E. ..... St. Cloud
Nietfield, Aloys B. ..... Sauk Centre
‡ O'Keefe, James P. ..... St. Cloud
‡ Olinger, John N. ..... St. Cloud
‡ Petersen, Robert T. ..... St. Cloud
‡ Phares, Otto C. ..... St. Cloud
Raetz, Sylvester J. ..... Maple Lake
Rice, William H. ..... St. Cloud
† Richards, William B. ..... St. Cloud
‡ Ritchie, Donald A. ..... St. Cloud
‡ Rovelstad, Roger A. ..... St. Cloud
‡ Rozycki, Anthony T. ..... St. Cloud
Salk, Richard J. ..... Albany
Schamber, Walter ..... St. Cloud

Continued on Next Page

Stearns-Benton County Medical Society *(Continued)*
Schmitz, Everett J. ....St. Cloud
Sisk, Harvey E. ....St. Cloud
‡ Slanga, Roger A. ....St. Cloud
‡ Smith, J. Weston ....St. Cloud
‡ Sommers, Stephen D. ....St. Cloud
‡ Stahn, Louis H. ....St. Cloud
‡ Stiles, Clifford D. ....Foley
Stuber, Robert R. ....St. Cloud
‡ Thienes, R. Lawrence ....St. Cloud
‡ Urbanyi, Eugene W. ....St. Cloud
Vanderpool, Thomas E. ....Paynesville
‡ Van Nostrand, David M. ....St. Cloud
‡ Veranth, Leonard A. ....St. Cloud
Warner, Paul L. ....St. Cloud
Wenner, Waldemar T. ....St. Cloud
Windschitl, Harold E. ....St. Cloud
‡ Wittrock, Louis H. ....St. Cloud
† Zachman, Albert H. ....Melrose
‡ Zeleny, Joseph H. ....St. Cloud

STEELE COUNTY MEDICAL SOCIETY

Steele County
Regular meetings, third Tuesday January, March, May, September and November
Annual meeting, November
Number of members 24

PRESIDENT
Honath, D. K. ....Owatonna
SECRETARY
Benjamin, R. J. ....Owatonna
‡ Anderson, Franklin C. ....Owatonna
Arnesen, John F. ....Owatonna
Benjamin, Roger J. ....Owatonna
‡ Buresh, Kenneth L. ....Owatonna
‡ deWerd, Robert W. ....Owatonna
Dewey, Donald H. ....Owatonna
Floersch, Adrian J. ....Owatonna
‡ Halvorsen, Daniel K. ....Owatonna
Hartung, Elmer H. ....Claremont
‡ Henry, John C. ....Owatonna
‡ Henry, Kenneth, G. ....Owatonna
‡ Hilker, Robert T. ....Owatonna
Honath, Donald H. ....Owatonna
Kulstad, Oscar S. ....Dodge Center
‡ Lundquist, Curt W. ....Owatonna
McEnaney, James E. ....Owatonna
† McIntyre, John A. ....Owatonna
† Morehead, Dewey E. ....Faribault
Nealy, Timothy E. ....Blooming Prairie
‡ Olson, Albert J. ....Owatonna
† Roberts, Oliver W. ....Owatonna
† Schaefer, Joseph F. ....Sun City, AZ
Stransky, Theodore W. ....Owatonna
† Wilkowske, Rudolph J. ....Owatonna

UPPER MISSISSIPPI MEDICAL SOCIETY

Aitkin, Cass, Crow Wing, Hubbard, Morrison, Todd & Wadena Counties
Regular meetings, January, April, September
Annual meeting, January
Number of members 82

PRESIDENT
Pelzl, Charles R. ....Pine River

SECRETARY
Anderson, Arden O. ....Brainerd
‡ Aga, John H. ....Brainerd
‡ Anderson, Arden O. ....Brainerd
Belcher, Royden A. ....Little Falls
‡ Bender, James H. ....Brainerd
‡ Bissinger, Lester L. ....Brainerd
Brown, Russell T. ....Browerville
Burman, Richard E. ....Aitkin
Cardle, George E. ....Brainerd
Closuit, Frederick C. ....Aitkin
‡ Coombs, Carl H. ....Cass Lake
‡ Crow, Earl R. ....Minnetonka
† Davis, Lloyd T. ....Wadena
Davis, Luther F. ....Wadena
Dimmick, Ivan C. ....Brainerd
‡ Dodson, Albertus F. ....Brainerd
Doty, Joseph ....Little Falls
† Erickson, Alvin O. ....Long Prairie
‡ Fitzsimons, William E. ....Brainerd
Fortier, George M. A. ....Little Falls
‡ Fortier, George M. A., Jr. ....Little Falls
‡ Gamm, Edgar R. ....Park Rapids
† Ghostley, Mary C. ....Bemidji
Grimes, Paul T. ....Park Rapids
Grose, Frederick N. ....Clarissa
Halme, William B. ....Wadena
Hansen, Milo L. ....Little Falls
Heid, James K. ....Little Falls
Hildreth, Thomas A. ....San Francisco, CA
Howard, David ....Long Prairie
Jacobson, Dennis R. ....Onamia
‡ Johnson, Douglas L. ....Brainerd
‡ Kanne, Earl R. ....Brainerd
Kelley, Roger E. ....Crosby
Knipp, William J. ....Brainerd
† Knoll, W. V. ....Brainerd
‡ Kussy, James C. ....Little Falls
Kvale, James V. ....Long Prairie
Larson, Donald R. ....Crosby
Larson, Theodore G. ....Brainerd
†‡ Lee, Hubert W. ....Brainerd
Lelwica, Thaddeus J. ....Staples
Lofstrom, Dennis ....Brainerd
Longfellow, Helen W. ....Brainerd
† Lund, Werner J. ....Staples
†‡ McLane, William O. ....Brainerd
Marshall, Clark M. ....Crosby
‡ Marvin, Joseph E. ....Brainerd
‡ Meller, Maurice ....Brainerd
‡ Mennis, William I. ....Staples
Montgomery, Guy E. ....Park Rapids
Morrison, Robert R. ....Park Rapids

Upper Mississippi Medical Society *(Continued)*

Mortenson, Howard O. ....Menahga
† Mosby, Maurice E. ....Long Prairie
Muesing, Mark A. ....Brainerd
Mulligan, Arthur M. ....Brainerd
‡ Muus, John H. ....Staples
Ness Duane E. ....Wadena
Nixon, James B. ....Crosby
Nordberg, Robert J. ....Little Falls
Olson, Lillian A. ....Ah-Gwah-Ching
Parker, Warren E. ....Sebeka
‡ Pedersen, Robert L. ....Brainerd
‡ Pelzl, Charles R. ....Pine River
Petraborg, Harvey T. ....Aitkin
Petterson, George R. ....USS Hope
Poppie, Robert W. ....Brainerd
†‡ Reichelderfer, Charles ....Staples
‡ Reichelt, Leland G. ....Wadena
Ringle, Otto F. ....Walker
Scanlon, Hugh A. ....Little Falls
Schmitt, Tim B. ....Browerville
Schulberg, Verne A. ....Minneapolis
Seifert, Donald R. ....Little Falls
Soriano, Dominador B. ....Onamia
Sosey, Walter K. ....Crosby
Spieler, F. B. ....Pequot Lakes
†‡ Stein, Raymond J. ....Pierz
Stoy, Robert A. ....Little Falls
Thompson, Paul E. ....Long Prairie
Thompson, U. James ....Staples
‡ Vandersluis, Charles W. ....Minneota
Watson, Sidney W. ....Little Falls
Westley, Kent F. ....Little Falls
Wiger, Oliver E. ....Little Falls
Williams, Mervyn M. ....Ah-Gwah-Ching
Witter, Robert L. ....Wadena

WABASHA COUNTY MEDICAL SOCIETY

Wabasha County
Regular meetings, special call
Annual meeting first Thursday after first Monday in October
Number of members 11

PRESIDENT
Martin, Doreen ....Pepin, WI
SECRETARY
Bowers, R. N. ....Lake City
‡ Bouquet, Bertram J. ....Wabasha
‡ Bowers, Robert N. ....Lake City
‡ Ellis, Earl W. ....Elgin
‡ Feigal, Gary R. ....Lake City
‡ Gjerde, William P. ....Lake City
† Habein, Harold C. ....Palo Alto, CA
‡ Mahle, Donald G. ....Wabasha
Moline, Doreen Martin ....Pepin, WI
‡ Sontag, David W. ....Lake City
‡ Timm, Marvin E. ....Wabasha

WAKOTA MEDICAL SOCIETY

Washington and Dakota Counties
Regular meetings second Tuesday in each month
Annual meeting, June
Number of members 30

PRESIDENT
Zeller, Hector ....Hastings
SECRETARY
Diessner, A. W. ....Stillwater
‡ Bealka, Neil ....Stillwater
† Brabec, Paul F. ....Hastings
Canine, James L. ....So. St. Paul
Dale, Les N. ....Hastings
‡ deLeon, Ben ....Stillwater
‡ Diessner, Ardell W. ....Stillwater
† Eiden, Vera M. ....Afton
Fasbender, Herman T. ....Hastings
Foderick, John W. ....Hastings
† Holcomb, Joel T. ....Marine-on-the-St. Croix
Hunter, Murray H. ....Farmington
‡ Jenson, James E. ....Stillwater
‡ Johnson, O. Guy ....St. Paul
‡ Juergens, Manley F. ....Stillwater
† Just, Herman J. ....Hastings
‡ Kiolbasa, Edward B. ....Stillwater
* Kulzer, Norbert J. ....Hastings
‡ McCarten, Francis M. ....Stillwater
Midboe, Gilbert T. ....Forest Lake
‡ Murphy, Thomas R. ....Stillwater
Peikert, Carl F. ....Forest Lake
Reid, James W. ....So. St. Paul
Ruggles, George M. ....Forest Lake
Sandkamp, Virgil ....So. St. Paul
‡ Schulz, Jerome E. ....Stillwater
Schwartz, Carl ....Hastings
† Sherman, Carnot H. ....Bayport
‡ Stratte, Jon R. ....Stillwater
† Van Meier, Henry ....Stillwater
Weiss, Carl A. ....Hastings
Zeller, Hector ....Hastings

WASECA COUNTY MEDICAL SOCIETY

Waseca County
Regular meeting, January
Annual meeting, January
Number of members 6

PRESIDENT
Olds, George H. ....New Richland
SECRETARY
Gray, Mark A. ....Waseca
Davis, Raymond D. ....Stockton, CA
‡ Dey, James W. ....Waseca
‡ Hergott, Patrick ....Waseca
‡ Hottinger, Raymond C. ....Janesville
‡ Normann, Stephen T. ....Waseca
‡ Oeljen, S. C. G. ....Waseca
‡ Olds, George H. ....New Richland
Pope, David A. ....Janesville

WEST CENTRAL MINNESOTA MEDICAL SOCIETY

Big Stone, Pope, Stevens and Traverse Counties
Regular meetings, third Tuesday in March, May,
September and November
Annual meeting, November
Number of members 21

PRESIDENT
Rossberg, R. A. ..... Morris
SECRETARY
Popoff, Russel G. ..... Graceville
£ Benjamin, Charles I. ..... St. Paul
† Bergan, Otto ..... Clinton
Bucher, Foster D. ..... Starbuck
£ Christenson, Carl E. ..... New Brighton
Colago, Victor M. ..... Browns Valley
Eide, O. A. ..... Hancock
Hedemark, Homer H. ..... Ortonville
† Hedemark, Truman A. ..... Ortonville
Karn, Jacob F. ..... Ortonville
Knip, Robert J. ..... Ortonville
Kooda, Jennings C. ..... Morris
Kozel, William J. ..... Morris
Lee, Gordon E. ..... Glenwood
Merrill, Robert ..... Des Moines, IA
Pettko, Joseph ..... Wheaton
Poole, James ..... Wheaton
Popoff, Russel G. ..... Garceville
Rossberg, Raymond A. ..... Morris
Swedenburg, Paul A. ..... Glenwood
Watson, Robert M. ..... Morris
Zempel, Alan R. ..... Starbuck

WINONA COUNTY MEDICAL SOCIETY

Winona County
Regular meetings, second Tuesday in January, April,
July and October
Annual meeting, January
Number of members 35

PRESIDENT
Finkelnburg, W. O. ..... Winona
SECRETARY
Heise, Herbert vR. ..... Winona
‡ Andersen, Horace J. ..... Winona
†‡ Christensen, Eli E. ..... Winona
‡ Degallier, Daniel ..... Winona
‡ Edin, Andrew E. ..... Winona
‡ Fenske, Arnold ..... Winona
Finkelnburg, William ..... Winona
‡ Garber, George L. ..... Winona
‡ Haesly, Warren W. ..... Winona
‡ Hartwich, Roger F. ..... Winona
‡ Hawk, Dale J. ..... St. Charles
Heise, Carl vR. ..... Winona
‡ Heise, Herbert vR. ..... Winona
‡ Heise, Paul vR. ..... Winona
Heise, William vR. ..... Winona
‡ Herland, Alexander L. ..... Winona
Hick, John F. ..... Winona
‡ Hughes, Sidney O. ..... Winona
‡ Johnson, Curtis M. ..... Winona
‡ Johnston, Leonard ..... Winona
†‡ Mattison, Percy A. ..... Winona
† Meinert, Albert E. ..... Winona
‡ Mulrooney, John G. ..... Winona
‡ Peterson, John R. ..... Rushford
‡ Roemer, Henry J. ..... Winona
‡ Rogers, Charles W. ..... Winona
Schafer, Charles F. ..... Winona
† Schmidt, Hilmar R. ..... Winona
‡ Testor, James V. ..... Winona
‡ Tweedy, John A. ..... Winona
‡ Tweedy, Robert B. ..... Winona
‡ Vieiralves, G. M. ..... Winona
‡ Weiss, Joseph E. ..... Winona
‡ Wilmot, Thomas M. ..... Winona
Wilson, L. J. ..... Rushford
† Wilson, R. H. ..... Winona
†‡ Younger, Lewis I. ..... Winona

WRIGHT COUNTY MEDICAL SOCIETY

Wright County
Regular meetings, first Tuesday of every other month
Annual meeting in November
Number of members 17

PRESIDENT
Sandeen, Robert M. ..... Buffalo
SECRETARY
Shin, Rok ..... Howard Lake
‡ Anderson, Waldo P. ..... Buffalo
‡ Bendix, Lester H. ..... Annandale
‡ Bentzin, C. K. ..... Monticello
Cady, Timothy J. ..... Buffalo
‡ Catlin, Theodore J. ..... Buffalo
†‡ Ellison, Frank E. ..... Monticello
‡ Greenfield Theodore ..... Champlin
‡ Guilfoile, Pierre J. ..... Delano
†‡ Hart, William E. ..... Monticello
‡ Maus, Donald J. ..... Monticello
Mintalar, Jose M. ..... Winsted
‡ Ourada, Anthony L. ..... Maple Lake
‡ Purves, G. Harland ..... Buffalo
‡ Sandeen, Robert M. ..... Buffalo
‡ Shin, Rok ..... Howard Lake
‡ Smorstok, Matthew B. ..... Monticello
‡ Steiner, Andrew M. ..... St. Michael
†‡ Thielen, R. D. ..... New Brighton
‡ Whitesell, L. A., Jr. ..... Buffalo
‡ Zapf, John D. ..... Monticello

ZUMBRO VALLEY MEDICAL SOCIETY

Olmsted, Houston, Fillmore and Dodge Counties
Regular meetings, first Wednesday of every odd-numbered month
Annual meeting, November
Number of members 920

PRESIDENT
Bartholomew, Lloyd G. ..... Rochester

SECRETARY
Burke, Edmund C. ..... Rochester

EXECUTIVE SECRETARY
Fricke, Robert E. ..... Rochester

ASSOCIATE DIRECTOR
Jackman, Raymond J. ..... Rochester

‡ Aaro, Leonard A. ..... Rochester
£ Abboud, Charles F. ..... Rochester
£ Abboud, Nabil ..... Rochester
‡ Adson, Martin A. ..... Rochester
‡ Affeldt Daniel E. ..... Kasson
£ Aguilo, Juan J. ..... Rochester
£ Ahlfs, Jacob J. ..... Minnetonka
‡ Ahmann, David L. ..... Rochester
‡ Andersen, Howard A. ..... Rochester
‡ Anderson, Carl F. ..... Rochester
£‡ Anderson, James A. ..... Rochester
† Anderson, Mark J. ..... Sun City, AZ
‡ Anderson, Markham J., Jr. ..... Rochester
Anderson, Michael D. ..... FPO, San Francisco, CA
‡ Anderson, Milton W. ..... Rochester
£ Anderson, Richard D. ..... Rochester
‡ Andreini, Paul H. ..... Rochester
£ Angelini, Corrado I. ..... Rochester
£ Applestein, Bruce ..... Rochester
£ Ascough, Bruce M. ..... Rochester
Baars, Conrad ..... Rochester
‡ Baggenstoss, Archie H. ..... Rochester
£‡ Bailly, Richard C. ..... Rochester
†‡ Bair, Hugo L. ..... Rochester
Baird, Raymond L. ..... Reno, NV
¶ Bajec, Dusan ..... Belgrade, Yugoslavia
† Baker, George S. ..... Rochester
† Baker, Harry R. ..... Hayfield
‡ Baker, Hillier L., Jr. ..... Rochester
Balfour, William M. ..... Lawrence, KS
‡ Banfield, Frederick D. ..... Rochester
‡ Banner, Edward A. ..... Rochester
Baran, Ernest M. ..... San Francisco, CA
£ Barnes, Nicholas D. ..... Rochester
‡ Barry, Maurice J., Jr. ..... Rochester
£ Barrington, Bert ..... Rochester
‡ Bartholomew, Lloyd G. ..... Rochester
£ Baumer, Robert J. ..... Rochester
‡ Bayrd, Edwin D. ..... Rochester
‡ Beabout, John W. ..... Rochester
‡ Beahrs, Oliver H. ..... Rochester
Bechamps, Gerald J. ..... Ft. Meade, MD
Beckenbaugh, Robert D. ..... Ft. Hood, TX
£ Becker, Paul W. ..... Rochester
£ Beckley, James M. ..... Rochester
Beeckler, Donald C. ..... Fort Dix, NJ
‡ Belau, Paul G. ..... Rochester
£ Belcher, Darrell C. ..... Rochester
‡ Bennett, Clayton J. ..... Rochester
£ Benson, Ralph C., Jr. ..... Rochester
‡ Berge, Kenneth G. ..... Rochester
£‡ Berkman, John M. ..... Rochester
£ Bernstein, Sidney S. ..... Rochester
£ Berquist, Thomas H. ..... Rochester
£ Bertagnoll, Alfred P. ..... Rochester
£ Besson, Augustin ..... Lausanne, Switzerland
Beuret, Lawrence J. ..... Rockford, IL
£ Beyerlein, Charles R. ..... Rochester
‡ Bianco, Anthony J., Jr. ..... Rochester
‡ Bickel, William H. ..... Rochester
‡ Bisel, Harry F. ..... Rochester
‡ Black, B. Marden ..... Rochester
‡ Black, Leo F. ..... Rochester
£ Blanco-Benavides, Roberto ..... Rochester
£ Bocala, Romeo R. ..... Rochester
£ Bodell, Leonard S. ..... Rochester
Bonebrake, Robert A. ..... Gurnee, IL
£ Born, Michael P. ..... Rochester
£ Bowen, Thomas L. ..... Rochester
£‡ Boyd, David A., Jr. ..... Rochester
£ Boyer, Andrew G. ..... Rochester
£ Braasch, William F. ..... Rochester
‡ Brandenburg, Robert O. ..... Rochester
Breivis, James S. ..... Spokane, WA
Brewster, Robert C. ..... Grand Forks, ND
£ Briddell, Dennis M. ..... Rochester
Brodhun, John C. ..... Rochester
£ Broe, Gerald A. ..... Rochester
† Brown, Alex E. ..... Bradenton, FL
‡ Brown, Arnold L. ..... Rochester
‡ Brown, Henry A. ..... Rochester
‡ Brown, Joe R. ..... Rochester
£‡ Brown, Philip W. ..... Rochester
‡ Brown, Philip W., Jr. ..... Rochester
£ Brown, Robert S. ..... Rochester
Brown, Stephen R. ..... Rochester
£ Brown, Warwick L. ..... Rochester
Brubaker, Richard F. ..... Rochester
£ Bruner, Kenneth W., Jr. ..... Rochester
£ Bryan, James W. ..... Rochester
‡ Bryan, Richard S. ..... Rochester
£ Brzica, Stephen M., Jr. ..... Rochester
£ Buckley, John P. ..... Rochester
¶ Buchholz, Roger M. ..... Rochester
£ Buie, Louis A. ..... Rochester
‡ Burgert, E. O., Jr. ..... Rochester
‡ Burich, Harry F. ..... Rochester
‡ Burke, Edmund C. ..... Rochester
£ Burns, John T. ..... Rochester
Bush, David J. ..... Biloxi, MI
‡ Butt, Hugh R. ..... Rochester
£ Buza, Robert C. ..... Rochester
£ Buzanowski, Krystayna ..... Rochester
£ Byer, David E. ..... Rochester
£ Cabanela, Miguel E. ..... Rochester
‡ Cain, James C. ..... Rochester
‡ Callahan, John A. ..... Rochester
£ Callaway, Clifford W. ..... Rochester
£ Camacho, Luis-Guillermo ..... Rochester
‡ Cameron, Alan J. ..... Rochester
£ Campa, Herman K. ..... Rochester
‡ Campbell, Donald C. ..... Rochester
£ Campbell, John T. ..... Rochester
‡ Campbell, Malcolm K. ..... Rochester

Continued on Next Page

Zumbro Valley Medical Society *(Continued)*

£ Cannon, Patrick J. ..... Rochester
£ Carder, George A. ..... Rochester
‡ Carlson, Harley C. ..... Rochester
Carnahan, Charles E. ..... Grandview, MO
Carney, Francoise M. T. ..... Rochester
Carr, David T. ..... Rochester
‡ Carryer, Haddon M. ..... Rochester
‡ Carter, Earl T. ..... Rochester
£ Carter, M. Gary ..... Rochester
£ Cassan, Stanley M. ..... Stanford, CA
£ Chiavetta, Stephen V., Jr. ..... Rochester
£ Chesebro, James H. ..... Rochester
£ Chidlow, Judd H. ..... Rochester
‡ Childs, Donald S., Jr. ..... Rochester
£ Ching, Ernesto ..... Rochester
£ Chisholm, David M. ..... Rochester
£ Christensen, Robert D. ..... Rochester
‡ Christensen, Norman A. ..... Rochester
‡ Christiana, Richard L. ..... Rochester
Chumbley, Lee C. ..... Patuxent, MD
£ Chychota, Norman N. ..... Rochester
£ Citron, Joseph ..... Rochester
‡ Clagett, O. Theron ..... Rochester
£ Clark, Edward C. ..... San Francisco, CA
£ Clark, Leslie W. ..... Manchester, IA
£ Clement, Denis L. ..... Rochester
£ Cloherty, Martin G. ..... Rochester
‡ Cody, D. Thane ..... Rochester
£ Cody, Michael C. ..... Rochester
£ Cofield, Robert H. ..... Rochester
£ Cohen, Manley ..... Long Beach, CA
‡ Colby, Malcolm Y., Jr. ..... Rochester
Coleman, Robert L. ..... Whiteman, AFB, MO
£ Colville, David S. ..... Rochester
£ Conley, Dean R. ..... Rochester
£ Conn, Richard L. ..... Rochester
†‡ Cook, Edward N. ..... Rochester
£ Cooke, Nelson R. ..... Rochester
£ Cooney, William P., III ..... Rochester
£ Cooper, George IV ..... Rochester
‡ Cooper, Talbert ..... Rochester
Cooperman, Avram M. ..... Wichita Falls, TX
‡ Corbin, Kendall B. ..... Rochester
£ Corrado, Angelini ..... Rochester
Corrigan, Cyril J. ..... Rochester
‡ Coventry, Markham B. ..... Rochester
£ Covington, Edward C. ..... Rochester
£ Crout, James E. ..... Rochester
£ Crowder, David F. ..... Rochester
£ Cullen, Joseph M. ..... Rochester
‡ Culp, Clyde E. ..... Rochester
‡ Culp, Ormond S. ..... Rochester
Cupps, Roger E. ..... Rochester
‡ Dahlin, David C. ..... Rochester
‡ Dale, Allan J. D. ..... Rochester
£ Daniel, Britt T. ..... Rochester
‡ Daugherty, Guy W. ..... Rochester
£ Daugherty, Thomas W. ..... Rochester
Dauphine, Richard T. ..... FPO, New York, NY
† Davis, Austin C. ..... Pompano Beach, FL
£ Davis, David L. ..... Rochester
‡ Davis, George D. ..... Rochester
£ Davis, Zev ..... Rochester
‡ Dearing, William H. ..... Rochester
¶ DeBus, Robert L. ..... Rochester
‡ Decker, David G. ..... Rochester
£ Deffner, Norman F. ..... Rochester
£ DeMeester, Lee J. ..... Rochester
‡ DeRemee, Richard A. ..... Rochester
£ Derbenwick, Kenneth P. ..... Rochester
£ Derbenwick, Mary Jane ..... Rochester
‡ DeSanto, Lawrence W. ..... Rochester
£ de Souza e Silva, Nelson A. ..... Rochester
Detenbeck, Lee C. ..... Rochester
‡ Devine, Kenneth D. ..... Rochester
Devloo, Robert A. ..... Rochester
‡ DeWeerd, James H. ..... Rochester
‡ Didier, Edward P. ..... Rochester
£ Diaz-Buxo, Jose A. ..... Rochester
‡ Diessner, G. Roy ..... Rochester
‡ Dinapoli, Robert P. ..... Rochester
Dines, David E. ..... Rochester
£ Disney, Thomas F. ..... LaJolla, CA
£ Djalilian, Mohsen ..... Rochester
¶ Dobbins, Ronald V. ..... Rochester
£ Dobmeier, Lawrence J. ..... Rochester
‡ Dobyns, James H. ..... Rochester
‡ Dockerty, Malcolm B. ..... Rochester
£ Donoghue, Edmund R., Jr. ..... Rochester
‡ Donoghue, Francis E. ..... Rochester
£ Doris, Peter E. ..... Rochester
‡ Douglass, Bruce E. ..... Rochester
£ Downey, Gale T. ..... Rochester
Doyle, James R. ..... Rochester
£ Dozois, Roger R. ..... Edinburgh, Scotland
£ Drijanski, Ruben ..... Rochester
£ Driscoll, Thomas P. ..... Rochester
† Drips, Della G. ..... Rochester
‡ Duane, Drake D. ..... Rochester
£ DuBoff, Stuart M. ..... Rochester
£ DuBois, David D. ..... Rochester
£ Dumesnil, Jean G. ..... Rochester
£ Dupree, Emmett L., Jr. ..... Rochester
£ Durie, Brian G. M. ..... Rochester
‡ Dyck, Peter J. ..... Rochester
‡ Dyer, John A. ..... Rochester
£ Eckstein, John D. ..... Rochester
£ Egan, Ernest L. ..... Rochester
†‡ Elkins, Earl C. ..... Rochester
£ Ellerby, Richard A. ..... Rochester
£ Elliott, Charles M. ..... Rochester
£ Ellingsen, Norman H. ..... Rochester
Emerson, Robert K. ..... Laredo, TX
† Emmett, John L. ..... Rochester
£ Emmons, Patricia R. ..... Rochester
‡ Emslander, Richard F. ..... Rochester
Engelberg, Jerry ..... Fairfield, CA
Engle, Andrew G. ..... Rochester
£ Engels, Edward P. ..... Lexington, KY
‡ Erich, John B. ..... Rochester
‡ Erickson, Donald J. ..... Rochester
£ Erwin, Donald T. ..... Rochester
‡ Espinosa, Raul E. ..... Rochester
Ettinger, David S. ..... Ft. Leavenworth, KS
£ Etzell, Paul S. ..... Rochester
£ Evans, Titus C., Jr. ..... Rochester
‡ Faber, John E. ..... Rochester
‡ Facer, George W. ..... Rochester
£ Falcone, James ..... Rochester
£ Farrell, Kenneth H. ..... Rochester
†‡ Faulconer, Albert, Jr. ..... Rochester
£ Favrot, Laurence D. ..... Rochester
Fay, Thomas M. ..... Oakland, CA
Feldmann, Floyd M. ..... Lighthouse Point, FL
‡ Ferguson, Richard H. ..... Rochester

Zumbro Valley Medical Society *(Continued)*

†‡ Ferris, Deward O. ..... Rochester
£ Filbuch, Eugene E. ..... Rochester
Fink, Lawrence H. ..... Silver Springs, MD
£ Fink, Richard A. ..... Rochester
£ Fiore, Joseph P. ..... Rochester
‡ Fish, Charles R. ..... Rochester
£ Fitzgerald, Robert H., Jr. ..... Rochester
£ Fitzpatrick, Patrick J. ..... Rochester
Flanigan, Donald J. ..... Pensacola, FL
Flick, William F. ..... Cheyenne, WY
‡ Fontana, Robert S. ..... Rochester
£ Fordyce, Norman A. ..... Rochester
† Foss, Edward L. ..... Condon, MT
£ Foster, Thomas N., III ..... Rochester
‡ Foulk, William T., Jr. ..... Rochester
Fowler, Franklin S., Jr. ..... San Francisco, CA
Fraser, Richard A. ..... Rochester
£ Freedman, Harvey M. ..... Rochester
£ Freeman, Richard E. ..... Rochester
£ Freshman, John R. ..... Rochester
‡ Frethem, Allen A. ..... Rochester
† Fricke, Robert E. ..... Rochester
£ Frytak, Stephan ..... Rochester
‡ Furlow, William L. ..... Rochester
£ Fuster, Valentin ..... Rochester
Galloway, Jackson R. ..... Alexandria, LA
†‡ Gambill, Earl E. ..... Rochester
‡ Garber, James J. ..... Rochester
£ Gard, Joseph R. ..... Rochester
Garrick, James G. ..... Bethesda, MD
‡ Gastineau, Clifford F. ..... Rochester
Gedge, Stafford W. ..... Rochester
Gentling, Peter A. ..... APO San Francisco
£ Ghosh, Manas K. ..... Rochester
‡ Geraci, Joseph E. ..... Rochester
£ Gibbs, Marvin K. ..... Rochester
£ Gifford, William A. ..... Rochester
Gildersleeve, John W. ..... Charlotte Harbor, FL
£ Gillespie, Donald N. ..... Rochester
£ Gilsanz, Vicente ..... Rochester
£ Gismondi, Pedro A. ..... Rochester
Gisvold, John J. ..... Rochester
£ Goellner, John R. ..... Rochester
‡ Goldstein, Norman P. ..... Rochester
‡ Goldston, Edgar C. ..... Rochester
£ Goldyne, Marc Ellis ..... Rochester
‡ Good, C. Allen, Jr. ..... Rochester
£ Good, Andrew E. ..... Rochester
‡ Gorman, Columba A. ..... Rochester
‡ Gould, Allan B., Jr. ..... Rochester
£ Gould, Barry K. ..... Rochester
Gould, Ronauld J. ..... Anchorage, AL
‡ Grabow, Jack D. ..... Rochester
‡ Graf, John A. ..... Rochester
‡ Gravett, Desmond C. ..... Rochester
‡ Green, Paul A. ..... Rochester
‡ Greene, Laurence F. ..... Rochester
£ Greipp, Philip R. ..... Rochester
£ Greydanus, Donald E. ..... Rochester
Griffiths, Robert W. ..... El Paso, TX
‡ Groover, Robert V. ..... Rochester
£ Gross, Earl C. ..... Rochester
‡ Gross, John B. ..... Rochester
Grubbs, Larry T. ..... Rochester
£ Guller, Barbara ..... Rochester
£ Gura, George M., Jr. ..... Rochester
£ Haakenson, Robert C. ..... Rochester
£ Haddad, Paul G. ..... Rochester
‡ Hagedorn, Albert B. ..... Rochester
‡ Hahn, Richard G. ..... Rochester
†‡ Haines, Samuel F. ..... Rochester
†‡ Hallberg, Olav E. ..... Rochester
£ Hancock, William E. ..... Rochester
‡ Hanlon, David G. ..... Rochester
‡ Hanson, Norbert O. ..... Rochester
£ Hanson, Norman P. ..... Rochester
¶ Hanson, Phyllis ..... Rochester
£ Harder, Edward J. ..... Rochester
†‡ Hargraves, Malcolm M. ..... Rochester
† Harrington, Stuart W. ..... Rochester
‡ Hartfield, James E., Jr. ..... Rochester
¶ Hartmann, Ronald J. ..... Rochester
Havig, Terrance A. ..... Lubbock, TX
¶ Hauff, Karen J. ..... Rochester
Hayashi, Melvin M. K. W. ..... Belleville, IL
‡ Hayles, Alvin B. ..... Rochester
† Heck, Frank J. ..... Rochester
¶ Heidel, Werner ..... Rochester
Heimark, John J. ..... Mankato
† Heinberg, Charles E. ..... Rochester
† Helgason, Pall B. ..... Rochester
‡ Helmholz, Henry F., Jr. ..... Rochester
‡ Henderson, Edward D. ..... Rochester
‡ Henderson, John W. ..... Rochester
‡ Henderson, Lowell L. ..... Rochester
Hendricks, John L. ..... China Lake, CA
† Henderickson, Ronald R. ..... Rochester
Henke, Clarence E. ..... Rochester
‡ Hepper, Norman G. ..... Rochester
‡ Hermans, Paul E. ..... Rochester
† Hewitt, Edith S. ..... Rochester
‡ Hill, John R. ..... Rochester
‡ Hill, Richard W. ..... Rochester
Hines, Edgar A., Jr. ..... Brevard, NC
‡ Hoagland, H. Clark ..... Rochester
¶ Hodgin, Carol L. ..... Rochester
‡ Hodgson, John R. ..... Rochester
£ Hodgson, Stephen F. ..... Rochester
£ Hogan, William M. ..... Rochester
Holbrook, Margaret A. ..... Rochester
Holland, C. R. ..... Rochester
‡ Hollenhorst, Robert W. ..... Rochester
‡ Holman, Colin B. ..... Rochester
£ Horswill, Robert N. ..... Rochester
†‡ Horton, Bayard T. ..... Rochester
‡ Houser, Otis W. ..... Rochester
‡ Howard, Frank M., Jr. ..... Rochester
£ Howard, John D. ..... Rochester
‡ Howell, Llewelyn P. ..... Rochester
£ Hu, Chung-Hong ..... Rochester
£ Hudson, Albert W. ..... Rochester
£ Huerta, Enrique ..... Rochester
† Hunt, Arthur B. ..... Carnel, CA
‡ Hunt, James C. ..... Rochester
¶ Hunt, Max L., Jr. ..... Rochester
£ Huston, Kent A. ..... Rochester
£ Hynes, Kieran M. ..... Rochester
£ Ireland, Damian C. R. ..... Rochester
£ Irons, G. Benton ..... Rochester
£ Isaacson, Ronald ..... Rochester
£ Ivance, Richard J. ..... Rochester
‡ Ivins, John C. ..... Rochester
£ Jackman, Jane ..... Rochester
† Jackman, Raymond J. ..... Rochester
£ Jackman, Steven J. ..... Rochester
£ Jackson, Charles B. ..... Rochester
£ James, Reese E. ..... Rochester
Janda, Wayne E. ..... APO San Francisco, CA
£ Jander, Hartwig P. ..... Rochester

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Zumbro Valley Medical Society *(Continued)*

‡ Janes, Joseph M. ..... Rochester
£ Jilek, Dennis D. ..... Rochester
‡ Johnson, Carl E. ..... Rochester
‡ Johnson, Einer W., Jr. ..... Rochester
£ Johnson, Marvin W. ..... Rochester
* Johnson, Ralph B. ..... Lanesboro
£ Johnson, Thomas F. ..... Rochester
£ Johnson, Warren L., Jr. ..... Rochester
‡ Johnson, William J. ..... Rochester
£ Jones, H. Royden, Jr. ..... Rochester
£ Jones, Ian V. ..... Rochester
£ Jordan, James J. ..... Rochester
‡ Jorgensen, Edward O. ..... Rochester
‡ Joyce, John W. ..... Rochester
‡ Judd, Edward S. ..... Rochester
£ Juncos, Luis I. ..... Rochester
‡ Kaese, Werner E. ..... Rochester
£ Kahler, John G. ..... Rochester
£ Kaine, Richard F. ..... Rochester
£ Kaplan, Roy A. ..... Rochester
‡ Karnes, William E. ..... Rochester
‡ Kazmier, Francis J. ..... Rochester
£ Kearney, R. Wynn, Jr. ..... Rochester
‡ Kearns, Thomas P. ..... Rochester
†‡ Keith, Haddow M. ..... Rochester
† Keith, Norman M. ..... Rochester
Kelalis, Panayotis P. ..... Rochester
‡ Kelly, Patrick J. ..... Rochester
£ Kelman, Donald B. ..... Rochester
‡ Kennedy, Charles C. ..... Rochester
Kennel, Arthur J. ..... Kinshasa, Congo
£ Kepfer, Percy D. ..... Rochester
†‡ Kernohan, James W. ..... Rochester
‡ Kerr, Frederick W. L. ..... Rochester
£ Key, Samuel N., III ..... Rochester
‡ Kiely, Joseph M. ..... Rochester
‡ Kierland, Robert R. ..... Rochester
£ Killean, James E. ..... Rochester
£ Kim, Hyun-Hahk ..... Rochester
‡ Kimmel, George E. ..... Rochester
‡ Kincaid, Owings W. ..... Rochester
King, John E. ..... Ft. Worth, TX
£ Kipfer, Robert E. ..... Rochester
‡ Kirby, Thomas J. ..... Rochester
Kirklin, John W. ..... Birmingham, AL
Klass, Donald W. ..... Rochester
‡ Knutson, Lewis A. ..... Spring Grove
£ Kobayashi, Itsuro ..... Rochester
£ Kondo, Kiyotaro ..... Rochester
‡ Konicek, Robert G. ..... Rochester
¶ Kortz, Louise S. ..... Rochester
£ Koppers, Lawrence E. ..... Rochester
£ Koretzky, Emil D. ..... Rochester
¶ Kostick, Joseph ..... Rochester
Krigsten, Eli J. ..... Weisbaden, Germany
£ Krohn, John R. ..... Rochester
‡ Krupp, Neal E. ..... Rochester
£ Kuge, Mark T. ..... Rochester
£ Kuers, Peter F. W. ..... Rochester
£ Kuglitsch, John F. ..... Rochester
£ Kulak, Linton L. ..... Rochester
£ Kunert, Raoul T. ..... Rochester
Kvamme, Brynjulv ..... Mabel
‡ Kyle, Robert A. ..... Rochester
£ LaFlamme, George-Henri ..... Rochester
‡ Lake, Clifford F. ..... Rochester
£ Lanier, Anne P. ..... Rochester
£ Lanier, James F. ..... Rochester
£ Laventman, Jaime ..... Rochester
£ Lawrence, Robert D. ..... Rochester
£ Lazar, Anthony S. ..... Rochester
‡ Leary, Frank J. ..... Rochester
Leavelle, Dennis E. ..... San Antonio, TX
‡ Lee, Raymond A. ..... Rochester
#‡ Lee, Robert E. ..... Rochester
£ Leist, Frederick D. ..... Rochester
Leonard, Paul F. ..... Rochester
Levy, Jonathan M. ..... Albuquerque, NM
‡ Lillie, John C. ..... Rochester
¶ Lind, Judy E. ..... Rochester
‡ Lindsay, Malcolm I., Jr. ..... Rochester
‡ Linman, James W. ..... Rochester
£ Lippman, Harry H. ..... Rochester
† Litin, Edward M. ..... Hopkins
£ Little, John R. ..... Rochester
‡ Litzow, Thaddeus J. ..... Rochester
£ Lockwood, Reed R. ..... Rochester
‡ Lofgren, Eric P. ..... Rochester
‡ Lofgren, Karl A. ..... Rochester
‡ Logan, George B. ..... Rochester
£ Logan, William S. ..... Rochester
Long, John C. ..... Hadley, MA
£ Longstreth, George F. ..... Rochester
Loos, Gerald D. ..... APO New York, NY
†‡ Love, J. Grafton ..... Rochester
Lucas, Alexander R. ..... Rochester
£ Lucas, Charles T. ..... Rochester
‡ Ludes, Bernard F. ..... Rochester
£ Lund, Richard E. ..... Rochester
‡ Lynn, Hugh B. ..... Rochester
‡ McBean, James B. ..... Rochester
£ McBurney, P. Louis ..... Rochester
£ McCann, William D. ..... Rochester
‡ McConahey, William M., Jr. ..... Rochester
McCoy, Stephen H. ..... Rochester
£ McDonald, Thomas J. ..... Rochester
£ McDougall, John C. ..... Rochester
£ McDuffie, Richard W., Jr. ..... Rochester
£ McElfresh, Edward C. ..... Rochester
McGee, Hugh E., Jr. ..... Fort Lee, VA
‡ McGill, Douglas B. ..... Rochester
‡ McIlrath, Donald C. ..... Rochester
£ McIlroy, Gary T. ..... Rochester
£ McIntyre, Donald G. ..... Rochester
‡ McKenna, Charles H. ..... Rochester
£ McMullan, Mart ..... Rochester
¶ McShane, Sister M. Quentin ..... Rochester
‡ MacCarty, Collin S. ..... Rochester
£ MacCarty, Robert L. ..... Rochester
£ MacCarty, William C., III ..... Rochester
£ MacDade, Albert D. W. ..... Rochester
MacDonald, Charles J. ..... Portsmouth, VA
£ MacDonald, Vance D. ..... Rochester
MacLean, Alexander R. ..... Rochester
†‡ Magath, Thomas B. ..... Rochester
Magid, Gail A. ..... Santa Cruz, CA
‡ Maher, Frank T. ..... Rochester
£ Maish, George O., Jr. ..... Rochester
£ Malagelada, Juan R. ..... Rochester
£ Malek, Reza S. ..... Winston Salem, NC
‡ Malkasian, George D. ..... Rochester
£ Manesis, John G. ..... Rochester
‡ Mankin, Harold T. ..... Rochester
£ Manson, Roberto R. ..... Rochester
‡ Marcoux, J. Paul ..... Rochester

Zumbro Valley Medical Society *(Continued)*

£ Marik, Francis ..... Rochester
Marion, Dennis F. ..... Wright-Patterson AFB, OH
£ Marmer, Robert H. ..... Rochester
£ Marsiglia, Juan C. ..... Rochester
Martalock, Dean L. ..... Great Lakes, IL
‡ Martens, Theodore G. ..... Rochester
£ Martimbeau, Pierre ..... Rochester
‡ Martin, Gordon M. ..... Rochester
‡ Martin, Harold R. ..... Rochester
¶ Martin, James E. ..... Rochester
‡ Martin, John T. ..... Rochester
‡ Martin, Maurice J. ..... Rochester
£ Martin, Raymond A. ..... Rochester
£ Masserman, Richard L. ..... Rochester
† Masson, Duncan M. ..... Rochester
† Masson, James C. ..... Rochester
‡ Masson, James K. ..... Rochester
†‡ Mathieson, Don R. ..... Rochester
£ Mathison, Robert D. ..... Rochester
£ Matlak, Michael E. ..... Rochester
Matson, Roland W. ..... Spring Valley
Mayne, John C. ..... Rochester
£ Mendelson, Bryan C. ..... Rochester
‡ Merritt, Wallace A. ..... Rochester
‡ Messick, Joseph M. ..... Rochester
£ Metter, Earl J. ..... Rochester
Meyer, William C. ..... APO, New York, NY
£ Meyer, James J. ..... Rochester
Midyett, F. Allan ..... Memphis, TN
£ Miller, Joe I., Jr. ..... Rochester
‡ Miller, R. Drew ..... Rochester
‡ Miller, Ross H. ..... Rochester
‡ Miller, W. Eugene ..... Rochester
‡ Millikan, Clark H. ..... Rochester
‡ Mills, Stephen D. ..... Rochester
Mitchell, John C., III ..... Travis, AFB, CA
£ Mizalis, Athanasios J. ..... Rochester
† Moersch, Fred P. ..... Ft. Lauderdale, FL
† Moersch, Herman J. ..... Rochester
Moffitt, Emerson A. ..... Rochester
£ Mokri, Bahram ..... Rochester
‡ Molnar, George D. ..... Rochester
£ Monkman, George R. ..... Rochester
† Montgomery, Hamilton ..... Rochester
£ Moore, Barry B. ..... Rochester
£ Moore, Burton A. ..... Rochester
‡ Moore, Gordon L., II ..... Rochester
Mori, Hideo ..... Grand Meadow
£ Morimoto, Allen M. ..... Rochester
‡ Morlock, Carl G. ..... Rochester
‡ Morrow, George W., Jr. ..... Rochester
£ Morrey, Bernard F. ..... Rochester
‡ Morse, Robert M. ..... Rochester
£ Motto, Joseph D. ..... Rochester
Muhm, John R. ..... Lawton, OK
£ Mulcahy, John J. ..... Ann Arbor, MI
‡ Mulder, Donald W. ..... Rochester
£ Muller, Bernard J. ..... Rochester
‡ Muller, Sigfrid A. ..... Rochester
£ Murphy, Joseph W. ..... Rochester
Mussey, Mary Elizabeth ..... Rochester
Nathan, Fred F. ..... Ellsworth AFB, SD
£ Nauman, James C. ..... Rochester
‡ Neault, Roger W. ..... Rochester
£ Neel, H. Bryan, III ..... Rochester
£ Neinas, Frederick ..... Rochester
£ Nelson, Roger L. ..... Rochester
£ Nelson, Audrey M. ..... Rochester
£ Neupert, Jerrol R. ..... Rochester
‡ Nesset, David G. ..... Rochester
‡ Nicholas, Donald R. ..... Rochester
£ Nichols, Victoria R. ..... Rochester
£ Niedringhaus, Robert D. ..... Rochester
£ Nijensohn, Daniel E. ..... Rochester
£ Nisbet, William ..... Rochester
£ Niven, Robert G. ..... Rochester
£ Nolan, Declan R. ..... Rochester
£ Noller, Kenneth L. ..... Rochester
‡ Obetz, Samuel W. ..... Rochester
£ Odyniec, Norman A. ..... Rochester
O'Brien, Charles P. ..... Rochester
£ O'Hara, James P. ..... Rochester
‡ Olsen, Arthur M. ..... Rochester
Olson, Grant E. ..... West Concord
£ Olson, John D. ..... Rochester
‡ Olson, Neal R. ..... Rochester
‡ Onofrio, Burton M. ..... Rochester
† Onsgard, L. Kenneth ..... St. Petersburg, FL
£ Opel, D. Douglas ..... Rochester
£ Opgrande, John D. ..... Rochester
‡ Opitz, Joachim L. ..... Rochester
‡ Osmundson, Philip J. ..... Rochester
‡ Owen, Charles A., Jr. ..... Rochester
£ Oxman, Herbert A. ..... Rochester
£ Pairolero, Peter C. ..... Rochester
‡ Palumbo, Pasquale J. ..... Rochester
£ Paradis, Gaston R. ..... Rochester
‡ Parker, Robert L. ..... Rochester
† Parkhill, Edith M. ..... Rochester
£ Parry, Rodney R. ..... Rochester
Passmore, James A. ..... Seabrook, TX
¶ Patterson, Linda G. ..... Rochester
£ Patrick, Donald L. ..... Rochester
‡ Payne, W. Spencer ..... Rochester
† Pease, Gertrude L. ..... Rochester
‡ Perry, Harold O. ..... Rochester
‡ Perry, Lawrence B. ..... Rochester
‡ Peters, Gustavus A. ..... Rochester
† Petersen, Magnus C. ..... Rochester
‡ Peterson, Hamlet A. ..... Rochester
‡ Peterson, Lowell F. A. ..... Rochester
‡ Petit, Robert M. ..... Rochester
£ Petty, Roy W. ..... Rochester
£ Pfaffenbach, David D. ..... Rochester
‡ Peyla, Thomas L. ..... Rochester
£ Pien, Francis D. ..... Rochester
‡ Pierre, Robert V. ..... Rochester
£ Pikler, George M. ..... Rochester
£ Pliam, Michael ..... Rochester
‡ Pluth, James R. ..... Rochester
‡ Polley, Howard F. ..... Rochester
†‡ Pool, T. Lloyd ..... Rochester
£ Port, Friedrich K. ..... Rochester
‡ Poston, Lawrence M. ..... Caledonia
Pougiales, Mary L. ..... Rochester
£ Powell, David F. ..... Rochester
‡ Pozuelo-Utanda, Jose ..... Rochester
‡ Pratt, Joseph H., Jr. ..... Rochester
£ Prentice, Linda G. ..... Rochester
‡ Prentice, James A. ..... Rochester
†‡ Priestley, James T. ..... Rochester
£ Pritchard, Douglas J. ..... Rochester
‡ Pruitt, Raymond D. ..... Rochester
‡ Pugh, David G. ..... Rochester
‡ Purnell, Don C. ..... Rochester

Continued on Next Page

Zumbro Valley Medical Society *(Continued)*

£ Quiroz, Salvador E. ..... Rochester
£ Radtke, Wallace E. ..... Rochester
£ Rahimi, Abbas ..... Rochester
£ Raimundo, Hugh Sa ..... Rochester
‡ Ralston, Donald E. ..... Rochester
£ Ramos, Raul ..... Rochester
‡ Randall, Raymond V. ..... Rochester
£ Reckles, Lawrence N. ..... Rochester
‡ Reese, David F. ..... Rochester
£ Reick, Robert R. ..... Rochester
Reilly, William F., Jr. ..... Davis-Monthan AFB, AZ
‡ Reitemeier, Richard J. ..... Rochester
‡ ReMine, William H., Jr. ..... Rochester
‡ Restall, Charles J. ..... Rochester
Reynolds, James C. ..... San Antonio, TX
‡ Rhoton, Albert L., Jr. ..... Rochester
‡ Riggs, B. Lawrence ..... Rochester
Riley, Fenwick C., Jr. ..... Rochester
Risser, Alden F. ..... Stewartville
‡ Ritter, Donald G. ..... Rochester
‡ Rivan, Robert J. ..... Rochester
£ Rivers, Thomas A. ..... Rochester
‡ Robertson, Dennis M. ..... Rochester
£ Robertson, Robert C. ..... Rochester
£ Rodarte, Joe R. ..... Rochester
£ Rogers, John R. ..... Rochester
£ Rogers, Roy S., III ..... Rochester
‡ Rome, Howard P. ..... Rochester
‡ Rooke, E. Douglas ..... Rochester
£ Rosenbaum, Alan H. ..... Rochester
£ Rosenbaum, Robert A. ..... Rochester
‡ Rosenow, Edward C., III ..... Rochester
Rosevear, John W. ..... Minneapolis
‡ Ross, James V., Jr. ..... Rochester
£ Roth, George R., Jr. ..... Rochester
‡ Rovelstad, Randolph A. ..... Rochester
Roy, Paul H. J. ..... Quebec, Canada
†‡ Rucker, Charles W. ..... Rochester
£ Rue, David S. ..... Rochester
‡ Rushton, Joseph G. ..... Rochester
£ Russ, Homer H. ..... Rochester
£ Russell, Robert C. ..... Rochester
†‡ Rynearson, Edward H. ..... Rochester
£ Salanga, Virgilio D. ..... Rochester
‡ Salassa, Robert M. ..... Rochester
£ Samara, David J. ..... Rochester
‡ Sams, W. Mitchell, Jr. ..... Rochester
‡ Sander, Frank V., Jr. ..... Rochester
‡ Sanderson, David R. ..... Rochester
‡ Sandok, Burton A. ..... Rochester
£ Sanfelippo, Peter M. ..... Rochester
£ Satava, Richard M. ..... Rochester
Sauer, Robert L. ..... Preston
‡ Sauer, William G. ..... Rochester
£ Savoy, Leonard B. ..... Rochester
‡ Sawtell, Robert R. ..... Rochester
£ Scanlon, Edward S. ..... Rochester
‡ Scanlon, Paul W. ..... Rochester
£ Sciallis, Gabriel F. ..... Rochester
‡ Schirger, Alexander ..... Rochester
£ Schnur, Paul L. ..... Rochester
£ Schoenberg, Bruce S. ..... Rochester
‡ Scholz, Donald A. ..... Rochester
Schrantz, Robert D. ..... Rochester
£ Schroeder, James G. ..... Rochester
£ Schroeder, Stephen B. ..... Rochester
‡ Schroeter, Arnold L. ..... Rochester
Schutt, Allan J. ..... Rochester
Schutt, Ann H. ..... Rochester
£ Schwab, Peter M. ..... Rochester
¶ Schwartau, Neal W. ..... Rochester
¶ Schwerman, Earl A., Jr. ..... Rochester
¶ Scott, James J. ..... Rochester
£ Segal, Anthony ..... Rochester
£ Seghers, Victor K. ..... Rochester
£ Segura, Joseph W. ..... Rochester
†‡ Seldon, T. Harry ..... Rochester
£ Serafano, Donald N. ..... Rochester
‡ Sessler, Alan D. ..... Rochester
£ Shallal, John A. ..... Rochester
£ Shea, John A. ..... Rochester
£ Shearin, Robert P. N. ..... Rochester
£ Sheehan, William C. ..... Rochester
£ Shen, Fu-hsiung ..... Rochester
‡ Sheps, Sheldon G. ..... Rochester
Shertzer, John H. ..... Ft. Bragg, NC
‡ Shick, Richard M. ..... Rochester
£ Sidell, Peter M. ..... Rochester
‡ Siekert, Robert G. ..... Rochester
‡ Silverstein, Murray N. ..... Rochester
‡ Simons, John N. ..... Rochester
£ Simmons, Paul B. ..... Rochester
£ Singleton, Alice F. ..... Rochester
£ Sippe, Joseph L. ..... Rochester
£ Siqueira, Aristarco ..... Rochester
£ Sisco, William T. ..... Rochester
£ Sizemore, Glen W. ..... Rochester
Skaggs, Harold, Jr. ..... Travis AFB, CA
Skinner, Ira C., III ..... San Antonio, TX
£ Slocum, James L., Jr. ..... Rochester
£ Smigiel, Mitchell R., Jr. ..... Rochester
£ Smith, J. Baldwin III ..... Rochester
¶ Smith, Ray P. ..... Rochester
‡ Smith, Lucian A. ..... Rochester
‡ Smith, Ralph E. ..... Rochester
Smith, Ronald E. ..... Rochester
Smith, V. Roy ..... Rochester
Snyder, Robert E. ..... Spring Valley
£ Soderstrom, Carl W., Jr. ..... Rochester
£ Solley, Graham O. ..... Rochester
£ Somerville, Gordon W. ..... Rochester
£ Sondag, Glenn E. ..... Rochester
Sones, Donald A. ..... Rochester
£ Sonnemaker, Robert E. ..... Rochester
£ Soriya, Lashman ..... Rochester
‡ Soule, Edward H. ..... Rochester
£ Speirs, Harvey R. ..... Rochester
‡ Spencer, Robert J. ..... Rochester
‡ Spiekerman, Ralph E. ..... Rochester
£ Spil, Samuel ..... Rochester
‡ Spittell, John A., Jr. ..... Rochester
‡ Sprague, Randall G. ..... Rochester
£ Srikumpol, Ananta ..... Rochester
£ Staryk, Steven E., Jr. ..... Rochester
†‡ Stauffer, Maurice H. ..... Rochester
Stecker, Raymond H. ..... APO, NY
Steffee, William P. ..... Rochester
£ Stehr, Christian H. ..... Rochester
£ Stein, Paul S. ..... Rochester
£ Steiner, Terrence R. ..... Rochester
£ Steinfeld, Carroll M. ..... Rochester
‡ Steinhilber, Richard M. ..... Rochester
Stern, Berry L. ..... APO San Francisco, CA
£ Stevens, John C. ..... Rochester
£ Stewart, John W. ..... Rochester

Zumbro Valley Medical Society *(Continued)*

‡ Stickney, J. Minott ..... Rochester
‡ Stillwell, G. Keith ..... Rochester
†‡ Stilwell, George G. ..... Rochester
£ Stine, Harold E. ..... Rochester
£ Stocker, Michael A. ..... Rochester
£ Stone, Stephen P. ..... Rochester
£ Stonnington, Henry H. ..... Rochester
‡ Stroebel, Charles F., Jr. ..... Rochester
‡ Strong, Cameron G. ..... Rochester
£ Su, Philo S. ..... Rochester
£ Suh, Ku Won ..... Rochester
‡ Summerskill, William H. ..... Rochester
£ Sun, Nora C. J. ..... Rochester
‡ Sundt, Thoralf M., Jr. ..... Rochester
£ Sung, David T. W. ..... Rochester
£ Suros, Juan ..... Rochester
‡ Svien, Hendrik J. ..... Rochester
£ Swanson, Gene E. ..... Rochester
‡ Swanson, David W. ..... Rochester
£ Swint, Robert E. ..... Rochester
£ Switz, Donald M. ..... Rochester
£ Takahashi, Raymond M. ..... Rochester
£ Tajik, Abdul J. ..... Rochester
Tangedahl, Tim N. ..... Bismarck, ND
£ Tapia, Hugo R. ..... Rochester
‡ Taswell, Howard F. ..... Rochester
‡ Tauxe, Welby N. ..... Rochester
£ Teunis, Bernard S. ..... Rochester
Thomas, Juergen E. ..... Rochester
£ Thomas, William F., III ..... Rochester
¶ Thompson, Conrad O. ..... Rochester
† Thompson, Gershom J. ..... Rochester
£ Thompson, Robert R. ..... Rochester
£ Throckmorton, Tom D. ..... Rochester
‡ Thurber, Deloran L. ..... Rochester
£ Tiede, James J. ..... Rochester
†‡ Tillisch, Jan H. ..... Rochester
£ Tindel, Jerry R. ..... Rochester
‡ Tinkham, Robert G. ..... Rochester
£ Tinstman, Thomas C. ..... Rochester
Tompkins, Richard B. ..... Rochester
£ Totz, Robert S. ..... Rochester
Townsend, Gary L. ..... Abilene, TX
‡ Trautmann, James C. ..... Rochester
£ Tressler, Hubert A. ..... Rochester
£ Trowbridge, Arthur A., Jr. ..... Rochester
Tsairis, Peter ..... Bethesda, MD
£ Tschetter, Loren K. ..... Rochester
‡ Tyce, Francis A. ..... Rochester
† Uihlein, Alfred ..... Rochester
‡ Underdahl, Laurentius ..... Rochester
‡ Utz, David C. ..... Rochester
Utz, Philip H. ..... La Crosse, WI
£ Vanesak, Richard J. ..... Rochester
Van Dervoort, Robert L., Jr. ..... Carswell AFB, TX
¶ Van Groll, Sister Kathleen ..... Rochester
Van Herik, Martin ..... Rochester
Van Ness, W. Noel T. ..... Columbia, SC
† Van Ooyen, Marinus ..... Rochester
£ Vargas-Cortes, Fernando ..... Rochester
¶ Vergin, Marcia ..... Rochester
‡ Vaughn, Louis D. ..... Rochester
£ Villanueva, Javier P. ..... Rochester
Virnig, Hildegard J. ..... Caledonia
Wahner, Heinz W. ..... Rochester
¶ Wakim, Khalil G. ..... Terre Haute, IN
‡ Wallace, Robert B. ..... Rochester
£ Walser, Adolf H. ..... Rochester
†‡ Walters, Waltman ..... Rochester
‡ Ward, L. Emmerson ..... Rochester
† Watkins, Charles H. ..... Sun City, AZ
£ Webb, Maurice J. ..... Rochester
£ Webel, Max L. ..... Rochester
£ Weber, Edward R. ..... Rochester
Webster, Kirk H. ..... San Antonio, TX
‡ Weed, Lyle A. ..... Rochester
‡ Weeks, Richard E. ..... Rochester
£ Wegener, Lee T. ..... Rochester
Weick, James K. ..... Camp Lejeune, NC
†‡ Weir, James F. ..... Rochester
‡ Welch, John S. ..... Rochester
‡ Wellman, William E. ..... Rochester
Wellner, Theodore O. ..... Rochester
£ Welsch, John A. ..... Rochester
£ Welsh, George F. ..... Rochester
‡ Wente, Harold A. ..... Rochester
£ West, Thomas L. ..... Seattle, WA
£ Westmoreland, Barbara ..... Rochester
Westrup, John E. ..... Lanesboro
‡ Wharton, William P. ..... Rochester
‡ Whisnant, Jack P. ..... Rochester
£ White, Alan V. M. ..... Rochester
‡ White, Roger D. ..... Rochester
‡ White, William L. ..... Rochester
‡ Wilkowske, Conrad J. ..... Rochester
Williams, W. Byron ..... Charleston, SC
£ Williamson, Kenneth R. ..... Rochester
£ Willis, Larry F. ..... Rochester
†‡ Willius, Frederick A. ..... Rochester
£ Willvonseder, Robert ..... Rochester
£ Wilson, Charles S. ..... Rochester
‡ Wilson, David M. ..... Rochester
Wilson, M. Robert, Jr. ..... Faribault
‡ Wilson, Robert B. ..... Rochester
Wilson, Viktor O. ..... Minneapolis
‡ Wiltsie, John C. ..... Rochester
£ Winegardner, Galen E. ..... Rochester
‡ Winkelmann, Richard K. ..... Rochester
¶ Woida, Sharon F. ..... Rochester
£ Wolf, Richard J. ..... Rochester
‡ Wollaeger, Eric E. ..... Rochester
£ Wong, Freeman E. ..... Rochester
£ Wong, Terry C. Y. ..... Rochester
‡ Wood, Lloyd T. ..... Rochester
‡ Woods, John E. ..... Rochester
£ Woodward, Anthony H. ..... Rochester
‡ Woolner, Lewis B. ..... Rochester
‡ Worthington, John W., Jr. ..... Rochester
£ Wurtele, Lester H. ..... Rochester
£ Yon, Jerry Lee ..... Rochester
Yoss, Robert E. ..... Rochester
†‡ Young, Henry H. ..... Rochester
£ Yukl, Richard L. ..... Rochester
£ Zack, John P. ..... Rochester
£ Zujko, Richard D. ..... Rochester

ALPHABETIC ROSTER

Key to Symbols

* Deceased
† Associate and Life
£ Resident and Intern
§ Medical Student
Service
¶ Affiliate and Honorary

‡ Wife is Member of Women's Auxiliary

A

Aaro, Leonard A. ..... Rochester
£ Abboud, Charles F. ..... Rochester
£ Abboud, Nabil ..... Rochester
Abraham, Arden L. ..... Duluth
Abrams, Alexander, Jr. ..... St. Paul
Abrams, Donald J. ..... Shakopee
Abramson, Buron I. ..... Minneapolis
Abramson, Milton ..... Minneapolis
Abullarade, Jose A. ..... Minneapolis
Abuzzahab, Faruk S. ..... Minneapolis
Adair, Albert F., Jr. ..... St. Paul
Adams, Brandon L. W. ..... Minneapolis
Adams, Harold R. ..... St. Paul
Adams, Patrick J. ..... Shakopee
Adams, Richard I. ..... Minneapolis
Adcock, Leon L. ..... Minneapolis
Adicoff, Arnold ..... Minneapolis
Adkins, C. Douglas ..... Minneapolis
Adkins, James T. ..... Coon Rapids
Adson, Martin A. ..... Rochester
Affeldt, Daniel E. ..... Kasson
Aga, John J. ..... Brainerd
£ Aquilo, Juan J. ..... Rochester
Agustsson, Hreidar ..... Minneapolis
Ahern, Eugene E. ..... Minneapolis
† Ahlfs, Jacob J. ..... Avon
Ahlstrom, Robert C. ..... St. Paul
Ahmann, David L. ..... Rochester
Ahola, Kenneth E. ..... Hibbing
Ahrens, Curtis F. ..... Duluth
Ahrens, Robert M. ..... St. Paul
Akbar, Sajady ..... Minneapolis
Akhaven, Traz ..... Alexandria
Akins, Willard M. ..... Red Wing
Aksoy, Mustafa ..... St. Paul
Alari, Heino ..... Excelsior
Albrecht, Raymond J. ..... St. Paul
Alden, Charles W. ..... Kimball
Alden, John F. ..... St. Paul
* Alexander, Harlan A. ..... Minneapolis
Alexander, Paul J. ..... Hibbing
† Aling, Charles A. ..... Minneapolis
Alkon, Ellen ..... Minneapolis
Allen, James R. ..... Minneapolis
Allen, John H. ..... Montevideo
Allison, David D. ..... Litchfield
Alter, Milton ..... Minneapolis
Altman, Robert L. ..... St. Paul
Alton, Donald G. ..... St. Paul
Amatuzio, Donald S. ..... Minneapolis
Amerongen, Werner W. ..... St. Paul
Amra, Waleed ..... Chaska
Amren, Don P. ..... Minneapolis
Anderegg, Alfred F. ..... Minneapolis
Andersen, Horace J. ..... Winona
Andersen, Howard A. ..... Rochester
Andersen, James G. ..... Minneapolis
Andersen, Robert C. ..... Minneapolis
Anderson, Arden O. ..... Brainerd
Anderson, Arnold S. ..... Minneapolis
Anderson, Carl F. ..... Rochester
Anderson, Chester A. ..... Hector
Anderson, Chester A. ..... Madison
Anderson, Dale L. ..... St. Paul
Anderson, David M. ..... Minneapolis
Anderson, David P., Jr. ..... Austin
Anderson, David W. ..... St. Paul
† Anderson, Ernest R. ..... Minneapolis
Anderson, Frank J. ..... Minneapolis
Anderson, Franklin C. ..... Owatonna
Anderson, Harold J. ..... Austin
£ Anderson, James A. ..... Rochester
Anderson, James J. ..... St. Paul
Anderson, James M. ..... Duluth
Anderson, Jo E. ..... LeSueur
Anderson, John A. ..... Minneapolis
Anderson, John W. ..... Blue Earth
† Anderson, Karl W. ..... Excelsior
Anderson, Margaret C. ..... St. Paul
† Anderson, Mark J. ..... Sun City, AZ
Anderson, Markham J., Jr. ..... Rochester
Anderson, Michael D. ..... Rochester
Anderson, Milton W. ..... Rochester
Anderson, Oscar D. ..... Mankato
Anderson, Quentin N. ..... Minneapolis
£ Anderson, Richard D. ..... Rochester
† Anderson, Richard E. ..... Willmar
Anderson, Richard W. ..... St. Paul
Anderson, Richard W. ..... Minneapolis
Anderson, Roger E. ..... Minneapolis
Anderson, Roger L. ..... Minneapolis
Anderson, Russell H. ..... Virginia
Anderson, U. Schuyler ..... Ft. Snelling
Anderson, W. Robert ..... Minneapolis
Anderson, Waldo P. ..... Buffalo
Anderson, Wallace E. ..... Minneapolis
Anderson, William H. ..... Minneapolis
Anderson, William T. ..... Minneapolis
Andre, James C. ..... Minneapolis
† Andreassen, Einar C. ..... Minneapolis
Andreassen, Rolf L. ..... Minneapolis
Andreini, Paul H. ..... Rochester
Andresen, Karl d'A ..... Minneapolis
£ Angelini, Corrado ..... Rochester
Ankner, Frank J. ..... Minneapolis
Anonsen, Richard E. ..... Minneapolis
Anselment, Lois A. ..... Excelsior
Antolak, Stanley J., Jr. ..... St. Paul
Antonelli, Jordan J. ..... Hibbing
Antonow, Arthur M. ..... Virginia
£ Appelstein, Bruce ..... Rochester
*† Arends, Archabald L. ..... Minneapolis
Arensen, Paul M. ..... Mankato
Arenson, Jeffrey A. ..... Minneapolis
Arey, Stuart Lane ..... Minneapolis
Arhelger, Stuart W. ..... Minneapolis
Arko, Frank R. ..... Hibbing
Arlander, Clarence E. ..... Minneapolis
Arlander, Thomas R. ..... Minneapolis
Arling, Leonard S. ..... Minneapolis
Armin, David W. ..... Two Harbors
Arms, James J. ..... Minneapolis
Armstrong, Byron H. ..... Minneapolis
Armstrong, Ralph S. ..... Winnebago

† Arndt, Harry W. ..... Detroit Lakes
Arnesen, John F. ..... Owatonna
Arnesen, Paul M. ..... Mankato
† Arnold, Ann W. ..... Minneapolis
Arnold, Thomas B. ..... Minneapolis
Arny, Frederick D. ..... St. Paul
† Arny, Frederick P. ..... St. Paul
† Aruguete, Alayne ..... Sandstone
£ Ascough, Bruce M. ..... Rochester
Ashmore, Herbert C. ..... St. Paul
Asp, Donald S. ..... Milaca
Asta, Joseph J. ..... Duluth
† Athens, Alvin G. ..... Santa Barbara, CA
Atmore, William G. ..... Duluth
Aufderheide, Arthur C. ..... Duluth
Aughenbaugh, John W. ..... Minneapolis
Aulick, Ernest J. ..... Paynesville
Auran, David B. ..... St. Paul
Aurelius, J. Richards ..... St. Paul
Ausman, Duane R. ..... St. Paul
Austrian, Sol ..... St. Paul
Autrey, William A. ..... St. Cloud
Avant, Robert F. ..... Minneapolis
Avren, Barbara L. ..... Virginia
Azad, Manouchehr M. ..... Minneapolis

B

Baab, Gary H. ..... St. Paul
Baars, Conrad W. ..... Rochester
Babb, Frank S. ..... St. Paul
Bach, Jerome M. ..... Minneapolis
Backus, Byron C. ..... Cloquet
Backus, Lloyd B. ..... Minneapolis
Backus, Reno E. ..... Minneapolis
† Backus, Reno W. ..... Cloquet
Bader, J. L. ..... Slayton
Baggenstoss, Archie H. ..... Rochester
Baggenstoss, Osmond J. ..... Minneapolis
Bagley, Charles M. ..... Duluth
Bagley, Elizabeth C. ..... Duluth
Bagley, Russell W. ..... Minneapolis
Bah, Merle C. ..... St. Paul
Baich, Velemir M. ..... Coleraine
£ Bailly, Richard C. ..... Rochester
† Bair, Hugo L. ..... Rochester
Baird, Raymond L. ..... Harmony
¶ Bajec, Dusan ..... Poljane, Yugoslavia
*† Baken, Melvin P. ..... St. Paul
Baken, Melvin P., Jr. ..... Minneapolis
Baker, Abe B. ..... Minneapolis
Baker, C. Camak ..... Minneapolis
Baker, Chilton R., Jr. ..... St. Paul
Baker, Daniel R. ..... Anoka
† Baker, George S. ..... Rochester
† Baker, Harry R. ..... Hayfield
Baker, Hillier L., Jr. ..... Rochester
Baker, Jeannette L. ..... Fergus Falls
Baker, Lowell H. ..... Minneapolis
Baker, Milton E. ..... Minneapolis
Baker, Norman H. ..... Fergus Falls
Bakke, Arnold C. ..... Minneapolis
Bakkila, Henry E. ..... Duluth
Balce, Regino V. ..... St. Paul
Balcos, Emmanuel G. ..... Minneapolis
Balderson, Robert P. ..... Grand Rapids
Balfour, William M. ..... Lawrence, KS
Balkin, Samuel G. ..... Minneapolis
Balkins, John W. ..... Minneapolis
Ballantine, Jerome J. ..... St. Cloud
Balmer, Albert I. ..... Duluth
Balogh, Charles J. ..... Minneapolis
Bancroft, Burton R., Jr. ..... St. Cloud
Bandt, Calvin M. ..... Minneapolis
Banfield, Frederick ..... Rochester
† Bank, Harry E. ..... Minneapolis
Banner, Edward A. ..... Rochester
Banovetz, John D. ..... Minneapolis
Baraga, Anthony R. ..... Hibbing
Baran, Ernest M. ..... Beaver Meadows, PA
Barbarisi, Charles F. ..... Mankato
£ Barnes, Nicholas D. ..... Rochester
Barnes, Richard E. ..... Aurora
Barnett, Robert M. ..... Minneapolis
Barno, Alex ..... Minneapolis
Barr, Lowell C. ..... Albert Lea
Barr, Lowell W. ..... Albert Lea
Barr, Maxwell M. ..... Minneapolis
Barrett, Patrick J. ..... Minneapolis
£ Barrington, Bert ..... Rochester
Barron, Jesse J. ..... Minneapolis
† Barron, Moses ..... Beverly Hills, CA
Barry, George J. ..... Minneapolis
Barry, Maurice J., Jr. ..... Rochester
Bart, Bruce J. ..... Minneapolis
Bartholdt, H. Peter ..... Cook
Bartholomew, Lloyd G. ..... Rochester
Bartness, John E. ..... Albert Lea
Bartzen, Peter J. ..... Duluth
Basinger, Harold P. ..... Windom
† Basinger, Homer P. ..... Windom
Batdorf, B. Niles ..... Mankato
Bateman, Clarence V. ..... Fergus Falls
Bauer, Eugene L. ..... St. Paul
Bauman, John C. ..... Foley
£ Baumer, Robert J. ..... Rochester
Baumgartner, C. John ..... Minneapolis
Baumgartner, Florian H. ..... Albany
Bayrd, Edwin D. ..... Rochester
Beabout, John W. ..... Rochester
Beach, Northrop ..... Minneapolis
Beahrs, Oliver H. ..... Rochester
Bealka, Neil M. ..... Stillwater
Bean, Charles N. ..... Waconia
Beard, Archibald H., Jr. ..... Minneapolis
Beaton, J. Gordon ..... Northfield
Bechamps, Gerald J. ..... Fort Eustis, VA
Beck, Charles J. ..... No. St. Paul
Beckenbaugh, Robert D. ..... Fort Hood, TX
Becker, Frederic T. ..... Duluth
£ Becker, Paul W. ..... Rochester
Beckering, Gerrit ..... Edgerton
Beckering, Roland G. ..... Edgerton
£ Beckley, James M. ..... Rochester
Becklund, Roger W. ..... Minneapolis
Beckman, Donovan L. ..... St. Paul
Beeckler, Donald C. ..... Ft. Dix, NJ
Beek, Harvey O. ..... St. Paul

Beeman, John A. ..... Minneapolis
Beer, John J. ..... St. Paul
Behr, Orlo K. ..... Crookston
Beirstein, Samuel ..... Minneapolis
† Beiswanger, Richard H. ..... Edina
Belau, Paul G. ..... Rochester
£ Belcher, Darrell ..... Rochester
Belcher, Royden A. ..... Little Falls
Bell, Donald C. ..... Minneapolis
Bell, Harry M., Jr. ..... Duluth
Bellomo, James ..... St. Paul
Bellomo, John ..... Fairmont
Bellville, Titus P. ..... Minneapolis
Belshe, Joseph ..... St. Cloud
Belsito, Alphonso A. ..... St. Paul
Belz, Reinmar ..... St. Paul
Belzer, Meyer S. ..... Minneapolis
Bendel, Richard P. ..... Minneapolis
Bendel, William L., Jr. ..... Minneapolis
Bender, James H. ..... Brainerd
Bendix, Lester H. ..... Annandale
*† Benell, Otto E. ..... Britt
Benesh, Louis A. ..... Minneapolis
£ Benjamin, Charles I. ..... Glenwood
Benjamin, Edwin G. ..... Minneapolis
Benjamin, Harold G. ..... Minneapolis
Benjamin, Richard D. ..... Minneapolis
Benjamin, Robert B. ..... Minneapolis
Benjamin, Roger J. ..... Owatonna
† Benjamin, Walter G. ..... Pipestone
Bennett, Clayton J. ..... Rochester
Bensman, Alan S. ..... Minneapolis
£ Benson, Ralph C., Jr. ..... Rochester
Benthack, Elaine M. ..... Minneapolis
Bentz, Herman D. ..... Anoka
Bentzin, C. K. ..... Monticello
Berestka, Stephen J. ..... Minneapolis
Berg, Arnold M. ..... Thief River Falls
Berg, Clinton C. ..... Excelsior
Berg, John H., Jr. ..... Montgomery
† Bergan, Otto ..... Clinton
Bergan, Robert O. ..... Duluth
* Berge, Harry L. ..... Mora
Berge, Kenneth G. ..... Rochester
Berger, Alex G. ..... Minneapolis
Berger, Phil R. ..... St. Cloud
Bergersen, Dean H. ..... Arlington
Bergh, Allen V. ..... St. Paul
Bergh, George S. ..... Minneapolis
Bergh, Solveig M. ..... Minneapolis
Berglund, Alvin E. ..... Cambridge
Berglund, Eldon B. ..... Minneapolis
Bergquist, James R. ..... Minneapolis
Bergstrom, John G. ..... Cokato
Bergstrom, Ralph W., Jr. ..... Maple Plain
† Bergstrom, William J. ..... Minneapolis
† Berkman, John M. ..... Rochester
Berkwitz, Nathaniel J. ..... Minneapolis
Berman, David A. ..... Minneapolis
Berman, Reuben ..... Minneapolis
Bernal, Jorge ..... Virginia
Bernier, Merrill J. ..... No. St. Paul
Berns, Max H. ..... Duluth
Bernstein, Dorothy M. ..... Minneapolis
Bernstein, Irving C. ..... Minneapolis
£ Bernstein, Sidney S. ..... Rochester
† Bernstein, William C. ..... St. Paul
£ Berquist, Thomas H. ..... Rochester
Berris, Harold ..... Minneapolis
Berry, Ronald N. ..... Minneapolis
£ Bertagnoll, Alfred P. ..... Rochester
Berzins, Rainis ..... Minneapolis
† Bessesen, Alfred N. ..... Minneapolis
† Besson, Augustin ..... Rochester
Beuning, John B. ..... St. Cloud
Beuret, Lawrence J. ..... Rockford, IL
Bevis, William D. ..... Minneapolis
£ Beyerlein, Charles R. ..... Rochester
† Bianco, Anthony J. ..... Vero Beach, FL
Bianco, Anthony J., Jr. ..... Rochester
Bickel, William H. ..... Rochester
Bieger, R. Cyril ..... Minneapolis
Biery, M. Barbara ..... Minneapolis
† Bieter, Raymond N. ..... Minneapolis
Bieter, Thomas G. ..... St. Paul
Bigler, Earl E. ..... Perham
Bigler, Ivan E. ..... Perham
Bilgutay, Aydin M. ..... Minneapolis
Bilka, Paul J. ..... Minneapolis
Billings, Harry H. ..... Red Wing
Billman, Herbert R. ..... Minneapolis
Biltz, John F. ..... Red Wing
Binder, Manuel R. ..... Minneapolis
Birkebak, Roland C. ..... St. Paul
Birkey, Thomas G. ..... Montevideo
Bisel, Harry F. ..... Rochester
Bishop, James R. ..... Minnetonka
Bissinger, Lester L. ..... Brainerd
Bittick, Wilbur H. ..... Minneapolis
Bjornson, Robert G. B. ..... St. Paul
Black, B. Marden ..... Rochester
*† Black, Earl J. ..... St. Paul
Black, Leo F. ..... Rochester
Black, William A. ..... New Ulm
Blackard, Clyde E. ..... Minneapolis
Blackburn, Henry W., Jr. ..... St. Paul
Blackwell, Leonard ..... Glencoe
Blake, Allan J. ..... Hopkins
Blake, James A. ..... Hopkins
Blake, Paul S. ..... Minneapolis
£ Blanco-Benavides, Roberto ..... Rochester
* Bloch, Henry S. ..... Minneapolis
Bloedel, Traugott J. ..... Osseo
Blomberg, Robert D. ..... Minneapolis
Blomberg, William R. ..... St. Paul
Bloom, David ..... Minneapolis
† Bloom, Joseph ..... Pompano Beach, FL
Bloom, Norman B. ..... Minneapolis
Blum, Clifford J. ..... Duluth
Blumberg, Henry B. ..... St. Paul
Blumenthal, Malcolm N. ..... Minneapolis
Blumer, Arlo R. ..... Albert Lea
Boade, W. Allan ..... Mankato
Boardman, Dalmon V. ..... Winona
Boardman, Peter J. ..... Wayzata
Boardman, William J. ..... Minneapolis
£ Bocala, Romeo R. ..... Rochester
† Bock, Rolland A. ..... St. Paul
£ Bodell, Leonard S. ..... Rochester
Boecker, Bernhard ..... Duluth
Bofenkamp, Benjamin ..... Minneapolis
† Bofenkamp, Ferdinand W. ..... Luverne
† Boies, Lawrence R. ..... Hopkins
Boies, Lawrence R., Jr. ..... St. Paul
Boline, Clifford A. ..... Battle Lake
Boller, Max A. ..... Minneapolis
Bologna, Camillo V. ..... Moorhead
Bolt, Donald A. ..... Minneapolis
Bolz, J. Arnold ..... Grand Rapids

† Boman, Paul G. ..... Duluth
Boman, Peter L. ..... Duluth
Bonebrake, Robert A. ..... Gurnee, IL
Bonewell, George W. ..... Minneapolis
Bonello, Frank J. ..... St. Paul
Bonner, John L. ..... Grand Rapids
Boody, George ..... Cambridge
Boone, Ervin S. ..... Luverne
£ Borgerson, Arthur H. ..... Long Prairie
Borgerson, M. A. ..... Hanley Falls
Borman, Chauncey N. ..... Minneapolis
£ Born, Michael P. ..... Rochester
Borowicz, Leonard A. ..... Minneapolis
Borrud, Chester C. ..... Anoka
Bosland, Howard G. ..... Rochester
Bosley, Patrick ..... Balaton
† Bottolfson, B. T. ..... Moorhead
† Bouma, Lewis R. ..... St. Paul
Bouquet, Bertram J. ..... Wabasha
Bouthilet, Florence J. ..... Minneapolis
£ Bowen, Thomas L. ..... Rochester
† Bowers, Gordon G. ..... Excelsior
Bowers, Robert N. ..... Lake City
Bowlin, Paul F. ..... Minneapolis
† Boyd, David A., Jr. ..... Rochester
Boyd, Frank E. ..... Pipestone
£ Boyer, Andrew G. ..... Rochester
Boyer, Samuel H. ..... Duluth
Boyle, Francis J. ..... Springfield
† Boynton, Ruth E. ..... Miami, FL
† Boysen, Herbert ..... Madelia
† Boyum, Allan J. ..... Minneapolis
Bozanich, Milosh S. ..... St. Cloud
† Braasch, William F. ..... Rochester
† Barbec, Paul F. ..... Hastings
Brace, Ray I. ..... Clinton
Bradford, David S. ..... Minneapolis
Bradley, Jeanne B. ..... Minneapolis
Bradley, John G. ..... Minneapolis
Bradley, William E. ..... Minneapolis
Brady, Charles H., Jr. ..... Mankato
Brainard, John B. ..... St. Paul
*† Brand, William A. ..... Redwood Falls
Brandenburg Robert O. ..... Rochester
Brandt, Henry E. ..... Minneapolis
Bransford, Paul W. ..... Minneapolis
Bratholdt, James W. ..... Watertown
† Bratrud, Edward ..... Alexandria
Brattensborg, Henry J. ..... St. Cloud
Brauer, H. H. ..... Mankato
Brauer, William W. ..... Minneapolis
Braun, Ohrmundt C. ..... Grand Rapids
Braun, Rene ..... Minneapolis
Bray, Jerome L. ..... Thief River Falls
Bray, Philip N. ..... Duluth
Breen, John J. ..... St. Paul
Breitenbucher, Robert B. ..... Minneapolis
Breivis, James S. ..... Spokane, WA
† Brekke, Harvey J. ..... Minneapolis
† Brende, Joel O. ..... Topeka, KS
Brenk, Paul E. ..... Detroit Lakes
Brennan, Joseph G. ..... Minneapolis
Brettingen, Larry J. ..... Mora
Bretzke, Carl O. ..... Hutchinson
Brewster, Robert C. ..... Grand Forks, ND
£ Briddell, Dennis M. ..... Rochester
Briggs, John F. ..... St. Paul
Briggs, Thomas G. ..... White Bear Lake
Brigham, Charles F., Jr. ..... St. Cloud
Brill, Alice K. ..... Minneapolis
Brink, Adlai A. ..... Baudette
Brink, Donald M. ..... St. Peter
Briones, Bienvenido R. ..... Hopkins
Broadie, Thomas E. ..... St. Paul
Brockberg, Daryl G. ..... St. Paul
† Brockberg, James A. ..... St. Paul
Brodhun, John C. ..... Rochester
† Brodie, Walter D. ..... St. Paul
£ Broe, Gerald A. ..... Rochester
Broker, Henry M. ..... St. Cloud
Broman, Harold R., Jr. ..... No. St. Paul
Bromer, Michael D. ..... Minneapolis
Brooker, Warren J. ..... Duluth
† Brooks, Charles N. ..... Wayzata
† Brown, Alex E. ..... Brandenton, FL
Brown, Arnold L. ..... Rochester
Brown, Charles T. ..... St. Paul
Brown, Christopher J. ..... St. Paul
Brown, Cyrus C., Jr. ..... Duluth
Brown, Frank T. ..... St. Cloud
Brown, Glenn W. ..... Halstad
Brown, Hector M. ..... St. Paul
Brown, Henry A. ..... Rochester
Brown, James E., Jr. ..... St. Paul
Brown, James P. ..... St. Paul
Brown, James R. ..... Crookston
Brown, Joe R. ..... Rochester
Brown, John H. ..... Minneapolis
Brown, John M. ..... St. Paul
† Brown, Philip W. ..... Rochester
Brown, Philip W., Jr. ..... Rochester
£ Brown, Robert S. ..... Rochester
Brown, Russell T. ..... Browerville
£ Brown, Stephen R. ..... Rochester
Brown, Warwick L. ..... Rochester
Brown, William D., Jr. ..... Minneapolis
£ Brownfield, James A. ..... Minneapolis
Brubaker, Richard F. ..... Rochester
Bruhl, Heinz H. ..... Faribault
Bruhl, Martin G. ..... St. Paul
£ Bruner, Kenneth W. ..... Oronoco
£ Bruner, Kenneth W., Jr. ..... Oronoco
† Brusegard, James F. ..... Red Wing
£ Bryan, James W. ..... Rochester
Bryan, Richard S. ..... Rochester
£ Brzica, Stephen M., Jr. ..... Rochester
Bucher, Foster D. ..... Starbuck
¶ Buchholz, Roger M. ..... Rochester
Buchstein, Harold F. ..... Minneapolis
Buchwald, Henry ..... Minneapolis
† Buck, Frederick H. ..... Shakopee
£ Buckley, John P. ..... Rochester
Buckley, Joseph J. ..... Minneapolis
Buckley, Robert P. ..... Duluth
Buege, William ..... Albert Lea
Buesgens, Ralph H. ..... Waterville
Bugby, Robert D. ..... Minneapolis
Bugenstein, Robert H. ..... Minneapolis
† Buie, Louis A. ..... Rochester
Buie, Louis A., Jr. ..... Minneapolis
Bulinski, Theodore J. ..... St. Paul
Bulluck, Matthew H. ..... Duluth
Bundt, Robert E. ..... Minneapolis
Bunker, Bevan W. ..... Anoka
Buran, David J. ..... Minneapolis
Burchell, Howard B. ..... Minneapolis
Buresh, Kenneth L. ..... Owatonna
Burgert, E. O., Jr. ..... Rochester

Burich, Harry F. ....Rochester
Burke, Edmund C. ....Rochester
Burke-Strickland, Martha J. ....Minneapolis
Burkholder, Dayton D. ....Anoka
Burklund, Edwin C. ....St. Paul
Burlingame, David A. ....St. Paul
Burman, Richard E. ....Aitkin
* Burmeister, Richard O. ....St. Paul
Burnett, Joseph W. ....New Ulm
Burnham, Wesley H. ....Minneapolis
† Burns, Catherine ....Excelsior
Burns, John M. ....St. Paul
£ Burns, John T. ....Rochester
† Burns, M. A. ....Edina
Burseth, Edgar C. ....Mora
Burton, J. Richard ....St. Paul
Burton, Thomas P. ....Minneapolis
£ Bush, David J. ....Biloxi, MI
Bush, Robert P. ....St. Paul
Butler, John K. ....Cloquet
Butt, Hugh R. ....Rochester
Butwinick, Conrad S. ....St. Paul
† Butzer, John A. ....Mankato
£ Buza, Robert C. ....Rochester
£ Buzanowski, Krystyna ....Rochester
£ Byer, David E. ....Rochester
Byrne, William J. ....St. Paul

C

£ Cabanela, Miguel E. ....Rochester
Cable, Morris L. ....Minneapolis
† Cabot, Clyde M. ....Ft. Lauderdale, FL
Cadbury, Jane B. ....Mankato
Cady, Timothy J. ....Buffalo
Cain, Clark L. ....St. Paul
Cain, James C. ....Rochester
Cain, James H. ....Alexandria
Cairns, Robert J. ....Redwood Falls
Calin, S. Hartley ....Minneapolis
Callahan, John A. ....Rochester
£ Callaway, Clifford W. ....Rochester
£ Camacho, Luis-Guillermo ....Rochester
Cameron, Alan J. ....Rochester
Cameron, Bruce P. ....Minneapolis
† Cameron, Isabell L. ....Minneapolis
Camp, Ray J. ....Madison
£ Campa, Herman K. ....Rochester
Campaigne, Robert J. ....Duluth
Campbell, Denis V. ....Minneapolis
Campbell, Donald C. ....Rochester
£ Campbell, John T. ....Rochester
Campbell, Malcolm K. ....Rochester
Campbell, Marilyn R. M. ....Minneapolis
† Campbell, Orwood J. ....Minneapolis
£ Campbell, Ronald G. ....Minneapolis
Campion, Brian C. ....St. Paul
Campos, Amador C. ....Aurora
Canine, James L. ....So. St. Paul
£ Cannon, Patrick J. ....Rochester
Cant, Wilbur F. ....Red Wing
Capistrant, Terrance D. ....St. Paul
Card, William H. ....Minneapolis
£ Carder, George A. ....Rochester
Cardle, George E. ....Brainerd
Cardle, James G. ....Minneapolis
Cardle, John B. ....Minneapolis
Carlander, Lester W. ....Minneapolis
Carley, Richard B. ....St. Paul
Carlon, Donald L. ....Moorhead
Carlson, Carl E. ....Alexandria
Carlson, Charles V. ....Mound
Carlson, Curtis H. ....Minneapolis
Carlson, David J. ....Minneapolis
Carlson, Harley C. ....Rochester
Carlson, Homer J. ....Pelican Rapids
Carlson, John V. ....Westbrook
Carlson, Lawrence ....Minneapolis
Carlson, Lloyd E. ....Worthington
Carlson, Vernon J. ....Moorhead
Carnahan, Charles E. ....Columbia, MO
Carney, Francoise ....Rochester
Carr, David T. ....Rochester
Carr, William J. ....Minneapolis
Carrasco, Enrique ....Minneapolis
Carrier, Thomas C. ....Minneapolis
Carryer, Haddon M. ....Rochester
Carter, Earl T. ....Rochester
Carter, Kenneth R. ....Granite Falls
£ Carter, M. Gary ....Rochester
Carter, Robert E. ....Duluth
Carter, Robert G. ....Minneapolis
Carthey, Frank J. ....New Ulm
Caspers, Carl G. ....Minneapolis
Cass, Alexander S. ....St. Paul
£ Cassan, Stanley A. ....Rochester
Castle, Donald D. ....St. Paul
Catlin, Theodore J. ....Buffalo
Cauble, Charles F. ....Minneapolis
† Cavanor, Frank T. ....Minneapolis
Cavert, H. Mead ....Minneapolis
Cedarleaf, Cherry B. ....White Bear Lake
Ceder, Elmer T. ....Minneapolis
Cella, Joseph A. ....Minneapolis
Cervenka, Charles F. ....New Prague
Cervenka, John D. ....New Prague
Cesnik, Robert J. ....Sauk Rapids
Chadbourn, Wayne A. ....Minneapolis
Chalgren, William S. ....Mankato
Challman, S. Alan ....Minneapolis
Chandler, William M. ....Minneapolis
† Chatterton, Carl C. ....St. Paul
Chedister, Charles R. ....Minneapolis
Chermak, Francis G. ....Phoenix, AZ
Chervenak, William A. ....Marine-on-St. Croix
£ Chesebro, James H. ....Rochester
Chesler, Merrill D. ....Minneapolis
£ Chidlow, Judd H. ....Rochester
Child, Sherman B. ....Minneapolis
Childs, Donald S., Jr. ....Rochester
£ Chilgren, Keith V. ....Minneapolis
£ Ching, Ernesto ....Rochester
£ Chisholm, David M. ....Rochester
Chisholm, Tague C. ....Minneapolis
Chizek, David ....St. Paul
Choithani, C. M. ....Crookston
Chou, Shelley N. ....Minneapolis
£ Chiavetta, Stephen V., Jr. ....Rochester

Christensen, Clarence H. ..... Duluth
† Christensen, Eli E. ..... Winona
Christensen, Llewellyn E. ..... Minneapolis
Christensen, Norman A. ..... Rochester
£ Christensen, Robert D. ..... Rochester
£ Christenson, Carl E. ..... Brighton
Christenson, Leland R. ..... Maple Plain
Christians, Richard L. ..... Rochester
Christgau, Roger A. ..... Minneapolis
Christian, William L. ..... Minneapolis
Christiansen, Harold A. ..... Jackson
Chumbley, Lee C. ..... Patuxent River, MD
Chunn, Stanley S. ..... Willmar
Church, Gerald E. ..... Two Harbors
£ Chychota, Norman N. ..... Rochester
Cich, John A. .....
Ciriacy, Edward W. ..... Minneapolis
£ Citron, Joseph ..... Minneapolis
Clagett, O. Theron ..... Rochester
Clapp, Hubert D. ..... Crookston
† Clark, Edward C. ..... San Francisco, CA
Clark, Elizabeth A. (Mrs. Halbert) ..... Duluth
† Clark, Harry B. ..... St. Cloud
Clark, Ivan T. ..... Sun City, AZ
† Clark, Leslie W. ..... Manchester, IA
Clark, Malcolm D. ..... Minneapolis
Clark, Robert S. ..... Minneapolis
Clark, W. Bruce ..... St. Paul
Clarke, Dean T. ..... Faribault
Clarke, John W. ..... Waconia
Clay, Lyman B. ..... Minneapolis
Cleary, John ..... St. Paul
£ Clement, Denis L. ..... Rochester
Clifford, George W. ..... Alexandria
Clifford, Thomas M. ..... Silver Bay
† Clifton, Theodore A. ..... Hollywood, FL
Cline, David W. ..... Minneapolis
£ Cloherty, Martin G. ..... Rochester
Close, Gerald A. ..... Glencoe
Closuit, Frederick ..... Aitkin
Cochrane, Byron B. ..... St. Paul
Cochrane, Ray F. ..... Minneapolis
Coddon, Walter D. ..... St. Paul
Cody, D. Thane ..... Rochester
£ Cody, Michael C. ..... Rochester
Coe, John I. ..... Minneapolis
Coe, Robert O. ..... Virginia
£ Cody, Michael C. ..... Rochester
£ Cofield, Robert H. ..... Rochester
Cohan, Richard C. ..... Minneapolis
Cohen, Bernard A. ..... Minneapolis
Cohen, Ephraim B. ..... Minneapolis
Cohen, Henry W. ..... Wayzata
£ Cohen, Manley ..... Long Beach, CA
Cohen, Sumner S. ..... Minneapolis
Colago, Victor M. ..... Browns Valley
Colby, Malcolm Y., Jr. ..... Rochester
† Colby, Woodard L. ..... St. Paul
Cole, George A. ..... Albert Lea
Cole, James S. ..... Minneapolis
Cole, Wallace H. ..... St. Paul
Coleman, John B. ..... St. Paul
Coleman, Robert L. ..... Whiteman AFB, MO
Coleman, Thomas P. ..... Minneapolis
Coll, James J. ..... Duluth
Collins, Roger T. ..... Duluth
Colliton, Patrick A. ..... Moorhead
Colman, Edward L. ..... Fergus Falls
Colton, Roger S. ..... St. Paul
£ Colville, David ..... Rochester
Comfort, Thomas H. ..... St. Paul
£ Conley, Dean R. ..... Rochester
Conley, Robert H. ..... Mankato
Conlin, F. Dixon ..... Minneapolis
Conlon, Daniel C. ..... Minneapolis
£ Conn, Richard L. ..... Rochester
Connolly, Coleman J. ..... St. Paul
Connolly, Joseph P. ..... So. St. Paul
† Connor, Charles E. ..... St. Paul
£ Connor, David G. ..... San Francisco, CA
† Cook, Edward N. ..... Rochester
£ Cooke, Nelson R. ..... Rochester
Coombs, Carl H. ..... Cass Lake
£ Cooney, William P. ..... Rochester
Cooper, Charles C. ..... Moose Lake
£ Cooper, George IV ..... Rochester
Cooper, Jack M. ..... St. Paul
Cooper, John P. ..... Minneapolis
Cooper, Robert R. ..... Minneapolis
Cooper, Talbert ..... Rochester
Cooperman, Avram M. ..... Wichita Falls, TX
Cope, Hershel B. ..... Virginia
Corbin, Kendall B. ..... Rochester
† Corniea, Albert D. ..... Minneapolis
£ Corrado, Angelini ..... Rochester
Correa, Dale H. ..... Minneapolis
Corrigan, Cyril J. ..... Rochester
Corson, Wilfred A. ..... Minneapolis
Cortez, Daniel P. ..... Minneapolis
Cosgriff, James A., Jr. ..... Olivia
Cotton, Gerald E. ..... Duluth
Coulter, Harold E. ..... Minneapolis
† Countryman, Roger S. ..... Saratoga, CA
Courteau, Robert D. ..... Ginelo, Rhodesia
Coventry, Markham B. ..... Rochester
Coventry, William D. ..... Duluth
Covey, Kenneth W. ..... Moorhead
£ Covington, Edward C. ..... Rochester
Cowan, Donald W. ..... Minneapolis
Cowan, Gary A. ..... Duluth
Cowan, George M. ..... Duluth
Cowger, Robert C. ..... Farmington
Cox, Milton J. ..... Duluth
Cox, Russell L. ..... Estherville, IA
Coy, Douglas J. ..... Grand Rapids
Craig, David M. ..... St. Paul
Craig, M. Elizabeth ..... Minneapolis
Cram, Barclay M. ..... St. Paul
Cramer, Glen G. ..... New Brighton
† Cranmer, Richard R. ..... Laguna Hills, CA
Cranston, Robert W. ..... Minneapolis
Creevy, Charles D. ..... Minneapolis
Creps, James R. ..... Duluth
Cress, Thomas L. ..... St. Cloud
Crislip, George D. ..... Waconia
† Cronwell, Bernhard J. ..... Austin
£ Crossley, Kent B. ..... Newtonville, MA
£ Crout, James E. ..... Rochester
Crow, Earl R. ..... Minnetonka
Crow, George M. ..... International Falls
£ Crowder, David F. ..... Rochester
Crowley, James H. ..... St. Paul
Crowley, Leonard V. ..... Minneapolis
Crudo, Vincent D. ..... St. Paul
Crum, Arthur Z. ..... St. Paul
Crutchfield, Charles E. ..... St. Paul
Crutchfield, Susan E. ..... St. Paul
Cruz, Waldemar F. ..... Minneapolis
Cullado, Andrionico F. ..... Minneapolis

£ Cullen, Joseph M. ..... Rochester
Cullen, Robert M. ..... Elmore
Culligan, David E. ..... St. Paul
Culligan, John A. ..... St. Paul
Culligan, Leo C. ..... Minneapolis
Culp, Clyde E. ..... Rochester
Culp, Ormond S. ..... Rochester
Culver, Lucian G. ..... St. Paul
Cumming, Edward D. ..... St. Paul
Cumming, Robert J. ..... St. Cloud
Cundy, Donald T. ..... Minneapolis
Cupps, Roger E. ..... Rochester
Curran, John P. ..... Minneapolis
Cushing, Richard T. ..... Minneapolis
† Cutts, George ..... Minneapolis

D

Daehlin, Rolf ..... Fergus Falls
Dagg, Earl ..... Thief River Falls
Daggett, Donald R. ..... Minneapolis
Dahl, James C. ..... Minneapolis
† Dahl, John A. ..... Excelsior
Dahlin, David C. ..... Rochester
Dahlquist, LaRue ..... St. Cloud
Dahlstrom, Donald D. ..... Minneapolis
Dale, Allan J. D. ..... Rochester
Dale, Les N. ..... Hastings
Daly, Alfred E. ..... St. Paul
Damberg, Sheldon W. ..... St. Paul
£ Daniel, Britt ..... Rochester
† Daniel, Donald H. ..... Minneapolis
Daniel, Clarke G. ..... Minneapolis
Danielson, Lennox ..... Litchfield
Danoff, David ..... Minneapolis
Danyluk, Michael ..... Minneapolis
Dargay, Cyril P. ..... Rochester
£ Daugherty, Guy W. ..... Rochester
Daumann, Roy F. ..... Minneapolis
Dauphine, Richard T. ..... FPO, NY, NY
Davenport, Jay A. ..... Virginia
David, Reuben ..... Hopkins
Davidson, A. Dale ..... Duluth
Davidson, J. Duane ..... Thief River Falls
† Davis, Austin C. ..... Pompano Beach, FL
Davis, Curtis E. ..... Minneapolis
£ Davis, David L. ..... Rochester
Davis, Edward V. ..... St. Paul
Davis, Eunice A. ..... St. Paul
Davis, George D. ..... Rochester
† Davis, Lloyd T. ..... Wadena
Davis, Luther F. ..... Wadena
Davis, Michael W. ..... Minneapolis
Davis, Raymond D. ..... Stockton, CA
Davis, Thomas H. ..... Minneapolis
Davis, William I. ..... Moose Lake
£ Davis, Zev ..... Rochester
Dawson, Lorin D. ..... Worthington
Dawson, W. John, Jr. ..... Minneapolis
Dearing, William H. ..... Rochester
Deason, Keith B. ..... Chisago City
¶ DeBus, Robert L. ..... Rochester
Decker, Charles W. ..... Hibbing
Decker, David G. ..... Rochester
† Dedeker, Kenneth L. ..... Minneapolis
£ Deffner, Norman F. ..... Rochester
Degallier, Daniel ..... Winona
Deger, Grant E. ..... Fairchild, AFB, WA
Delahunty, John R. ..... Red Wing
deLeon, Buenaventura ..... Stillwater
Delzell, Allen W. ..... Minneapolis
De Marais, Lloyd C. ..... Hibbing
£ DeMeester, Lee J. ..... Rochester
Demo, Robert A. ..... Albert Lea
Derauf, Donald E. ..... St. Paul
£ Derbenwick, Kenneth P. ..... Rochester
£ Derbenwick, Mary June ..... Rochester
Derechin, William ..... St. Paul
DeRemee, Richard A. ..... Rochester
† de Souza e Silva, Nelson A. ..... Rochester
De Santo, Lawrence W. ..... Rochester
Detenbeck, Lee C. ..... Rochester
Deters, Donald C. ..... St. Paul
Deutsch, Robert J. ..... Duluth
Devine, Kenneth D. ..... Rochester
Devloo, Robert A. ..... Rochester
DeWeerd, James H. ..... Rochester
Deweese, Joel T. ..... Bemidji
Deweese, Wilford J. ..... Bemidji
deWerd, Robert W. ..... Owatonna
Dewey, Donald H. ..... Owatonna
Diamond, Robert A. ..... Minneapolis
Diaz-Buxo, Jose A. ..... Rochester
Dickinson, Paul B. ..... St. Paul
Dickman, Roy W. ..... Minneapolis
Didier, Edward P. ..... Rochester
Diefenbach, Eugene J. ..... Minneapolis
Diego, Benito B. ..... Fridley
† Diehl, Harold S. ..... New York, NY
Diehl, James J. ..... Minneapolis
Dieperink, Willem ..... St. Paul
Dierker, Heinrich A. ..... Minneapolis
Diessner, Ardell W. ..... Stillwater
Diessner, Grant R. ..... Rochester
† Diessner, Henry D. ..... Hopkins
Dillie, Donald E. ..... Litchfield
Dillenburg, Cyril J. ..... Crookston
Dimants, Janis, Jr. ..... Minneapolis
Dimmick, Ivan C. ..... Brainerd
Dinapoli, Robert P. ..... Rochester
Dines, David E. ..... Rochester
£ Disney, Thomas F. ..... Rochester, NY
† Dittrich, Raymond ..... St. Paul
£ Djalilian, Mohsen ..... Rochester
Doan, Robert E. ..... Wayzata
Dobbins, Ronald V. ..... Rochester
Dobbs, Richard L. ..... Duluth
Dobler, Manfred G. ..... Ely
£ Dobmeier, Lawrence J. ..... Rochester
† Dobrin, Dale T. ..... Minneapolis
Dobson, Mervin W. ..... Mankato
Dobyns, James H. ..... Rochester
Docherty, John A. ..... Edina
Dockerty, Malcolm B. ..... Rochester
Docksey, John W. ..... Willmar
Dodds, William C. ..... Detroit Lakes
Dodson, Albertus F. ..... Brainerd
Doebler, Myron I. ..... Mora

Doherty, Elmer M. ....New Prague
Dokken, James H. ....Windom
Doman, Victor W. ....Lakefield
Doms, Vernon A. ....Elbow Lake
† Donaldson, Charles S. ....St. Cloud
Donatelle, Edward P. ....Minneapolis
£ Donoghue, Edmund R., Jr. ....Rochester
§ Donehower, Ross C. ....St. Paul
Donoghue, Francis E. ....Rochester
Donovan, Daniel L. ....New Brighton
Dooley, Robert T. ....St. Paul
£ Doris, Peter E. ....Rochester
† Dorge, Richard I. ....Minneapolis
Dornbach, Robert A. ....Minneapolis
Dorsey, George C., Jr. ....Minneapolis
Dorsey, William E. ....Minneapolis
Doscherholmen, Alfred ....Minneapolis
Doty, Joseph ....Little Falls
Dougan, Jerome W. ....Minneapolis
Douglass, Bruce E. ....Rochester
Douglass, Jesse E. ....Canon Falls
do Vale, Joao M. ....Minneapolis
£ Downey, Gale T. ....Rochester
† Doxey, Gilbert L. ....Minneapolis
Doyle, James R. ....Rochester
£ Dozois, Roger R. ....Rochester
† Dredge, Thomas E. ....Minneapolis
Dredge, Thomas E., Jr. ....Minneapolis
Drexler, Charles J. ....Duluth
Drexler, George W. ....Blue Earth
Dreyling, Roger A. ....Eden Valley
£ Drijanski, Ruben ....Rochester
Drill, Frederick E. ....Minneapolis
Drill, Herman E. ....Hopkins
† Drips, Della G. ....Rochester
£ Driscoll, Thomas P. ....Rochester
Drucker, Franklin G. ....Bigfork
Duane, Drake D. ....Rochester
£ Du Boff, Stuart M. ....Rochester
£ Dubois, David D. ....Rochester
Dubois, Julian F. ....Sauk Center
Duerr, Eleanor E. ....St. Paul
Duffy, John L. ....Minneapolis
Dummer, Donald J. ....New Brighton
£ Dumesnil, Jean G. ....Rochester
Duncan, Donald A. ....Minneapolis
Duncan, James W. ....Moorhead
Dunham, Charles K. ....St. Paul
Dunkel, Thomas B. ....St. Louis Park
Dunlap, David J. ....Minneapolis
Dunlap, Earl H. ....Minneapolis
Dunn, James P. ....St. Paul
Dunn, Robert C. ....St. Paul
Dunstan, Paul L. ....Willmar
Dupont, Joseph A. ....Excelsior
£ Dupree, Emmett L. ....Rochester
£ Durie, Brain G. M. ....Rochester
Durkin, John L. ....St. Paul
Duryea, Willis M. ....Minneapolis
Duryea, Willis M., Jr. ....Minneapolis
Duthoy, Everette J. ....St. Paul
Duvall, Arndt J., III ....St. Paul
Dvorak, Benjamin A. ....Minneapolis
Dwan, Paul F. ....Minneapolis
† Dworsky, Samuel D. ....Minneapolis
Dwyer, John J. ....Duluth
Dyck, Peter J. ....Rochester
Dyer, John Allen ....Rochester
Dyrdal, Paul J. ....St. Paul
Dysterheft, Adolf F. ....Gaylord
Dzuibinski, Emil H. ....St. Cloud

E

* Earl, George A. ....St. Paul
Earl, John R. ....St. Paul
Earl, Stephan H. ....Minneapolis
Eaton, David B. ....Worthington
Eberley, Tobe S. ....Benson
Ebert, Richard V. ....Minneapolis
Eckdale, John E. ....Mankato
Eckerly, Jean R. ....Minneapolis
Eckert, Joseph F. ....Mankato
£ Eckman, Matthew J. ....Duluth
Eckman, Philip F. ....Duluth
Eckman, Philip L. ....Duluth
Eckman, Ralph J. ....Duluth
£ Eckstein, John D. ....Rochester
Eder, Walter P. ....Minneapolis
Edin, Andrew ....Minneapolis
Edmondson, Hugh A., Jr. ....Minneapolis
Edwards, Laura E. ....St. Paul
† Edwards, J. Willard ....St. Paul
Edwards, Jesse E. ....St. Paul
Edwards, Lloyd G. ....St. Paul
† Edwards, Richard B. ....St. Paul
Edwards, Thomas J. ....St. Paul
† Edwards, Walter G., Jr. ....Bethesda, MD
Edwardson, Phillip L. ....St. Paul
Eelkema, Herman H. ....St. Paul
Efteland, Myles E. ....Minneapolis
£ Egan, Ernest L. ....Rochester
Egge, Sanford G. ....Albert Lea
Eggert, Delmer C. ....Mankato
Eginton, Charles T. ....Fargo, ND
*† Ehrenberg, Claude J. ....Boca Raton, FL
† Ehrlich, S. Paul ....Minneapolis
Eich, Matthew A. ....Minneapolis
Eichelberger, Dale L. ....Willmar
Eichenlaub, John E. ....Minneapolis
Eichhorn, Edmund P., Jr. ....Minneapolis
£ Eichten, John G. ....Minneapolis
Eide, O. A. ....Hancock
† Eiden, Vera M. ....Afton
Eifrig, David E. ....Minneapolis
Eilers, Vincent E. ....St. Paul
Einsig, Mitchell J. ....Wayzata
z Eisenberg, M. Michael ....Minneapolis
Eisenman, Walter ....Hibbing
Eisenstadt, William S. ....Minneapolis
Eitel, George D. ....Minneapolis
Ekberg, Fred ....Detroit Lakes
Eklund, Carl D. ....Duluth
† Elkins, Earl C. ....Rochester
£ Ellerby, Richard A. ....Rochester
Ellertson, Leonard M. ....Albert Lea
Ellinger, Albert J. ....Willmar
£ Ellingsen, Norman H. ....Rochester

Ellingson, Richard B. ..... Minneapolis
Ellington, Anna L. ..... Minneapolis
Elliott, Charles M. ..... Rochester
Elliott, J. W. ..... Mankato
Ellis, Cassius M. C. ..... Minneapolis
Ellis, Earl W. ..... Elgin
Ellis, John C., Jr. ..... Minneapolis
Ellis, Ronald W. ..... St. Paul
Ellison, Evan S. ..... Minneapolis
† Ellison, Frank E. ..... Monticello
Ellwood, Paul M., Jr. ..... Minneapolis
Elumba, Teodoro V. ..... St. Paul
Emanuel, Karl W. ..... Duluth
† Emerson, Edward C. ..... St. Paul
Emerson, Edward C. ..... St. Paul
Emerson, Edwin E. ..... Osakis
Emerson, Robert K. ..... Laredo, TX
† Emmett, John L. ..... Rochester
£ Emmons, Patricia R. ..... Rochester
Emmons, Robert W. ..... St. Paul
† Emond, Joseph S. ..... Farmington
Emond, Joseph S., Jr. ..... Farmington
Emslander, Richard F. ..... Rochester
† Endress, Edward K. ..... St. Paul
*† Engberg, Edward J. ..... Faribault
Engebretson, Paul ..... Alexandria
Engel, Andrew G. ..... Rochester
Engel, Joseph P. ..... Minneapolis
Engel, William L. ..... Minneapolis
Engelberg, Jerry ..... Fairfield, CA
† Engels, Edward P. ..... Marshall
Engelsgjerd, Gerald L. ..... Duluth
Engelstad, Wendell P. ..... Eveleth
England, Rodney W. ..... St. Paul
Englund, Elvin F. ..... Minneapolis
*† Engstrand, Oscar J. ..... Minneapolis
Engstrom, E. Duane ..... Minneapolis
Engstrom, George ..... St. Peter
Engstrom, Robert B. ..... Mankato
Engwall, Richard L. ..... Minnetonka
Enroth, Oscar E. ..... St. Paul
Erdal, Ove A. ..... Albert Lea
Erich, John B. ..... Rochester
† Erickson, Alvin O. ..... Long Prairie
Erickson, Carlton ..... Lindstrom
* Erickson, Clifford O. ..... Minneapolis
Erickson, Donald J. ..... Rochester
Erickson, Donald L. ..... St. Paul
Erickson, Laurence F. ..... Minneapolis
Erickson, Myron E. ..... Minneapolis
*† Erickson, Reuben F. ..... Minneapolis
Erickson, Robert L. ..... Rosemount
Erickson, Vernon D. ..... Grand Rapids
Ericsson, Kermit C. ..... Cambridge
Erlanson, A. Cornell ..... St. Paul
Erling, Carl B. ..... St. Paul
£ Ersek, Robert A. ..... Minneapolis
Ersfeld, Murray P. ..... St. Paul
£ Erwin, Donald T. ..... Rochester
Eselius, Erik P. ..... Minneapolis
Esensten, Sidney ..... Minneapolis
Espelien, Alan D. ..... St. Cloud
Espinosa, Raul E. ..... Rochester
Estrem, Ralph L. ..... Fergus Falls
Estrem, Robert D. ..... Fergus Falls
Ettinger, David S. ..... Ft. Leavenworth, KS
£ Etzell, Paul S. ..... Rochester
Etzwiler, Donnell D. ..... Minneapolis
Eustermann, John J. ..... Mankato
† Evans, Edward T. ..... Minneapolis
£ Evans, Titus C., Jr. ..... Rochester
Evensta, John B. ..... Grand Rapids
Everhart, Clarence E., Jr. ..... Minneapolis
Everly, Stephan S. ..... Minneapolis
Evison, Emerson O. ..... Duluth
Ewens, George B. ..... Virginia

F

Faber, John E. ..... Rochester
Facer, George W. ..... Rochester
£ Falcone, James C. ..... Rochester
Fallon, Virgil T. ..... Minneapolis
Falls, John L. ..... Red Wing
Farber, Abigail F. ..... Minneapolis
Farber, Lawrence A. ..... Minneapolis
Farber, Roger E. ..... Minneapolis
Farley, Harrison H. ..... Minneapolis
Farr, John D. ..... St. Paul
£ Farrell, Kenneth H. ..... Rochester
Farrell, T. Edwin ..... Minneapolis
Fasbender, Herman T. ..... Hastings
Fauchald, Nils, Jr. ..... Red Wing
Faul, Bennie C. ..... Worthington
£ Faulconer, Albert, Jr. ..... Rochester
Faust, John H. ..... Northfield
£ Favrot, Laurence D. ..... Rochester
£ Fawcett, Arthur M. ..... Renville
Fawcett, Keith R. ..... Duluth
Fay, Thomas M. ..... Oakland, CA
Fedders, Skaidrite ..... Willmar
Fedor, Robert ..... Willmar
Fee, John G. ..... St. Paul
Fehr, Peter E. ..... St. Paul
Feigal, David W. ..... Wayzata
Feigal, Gary R. ..... Lake City
Feigal, William M. ..... Fairmont
Feinberg, Philip ..... Minneapolis
Feinberg, Samuel B. ..... Minneapolis
Felder, Davitt A. ..... St. Paul
Feldmann, Floyd M. ..... Pompano Beach, FL
Felion, Arthur J. ..... St. Paul
* Fellows, Manley F. ..... Duluth
Fenske, Arnold W. ..... Winona
Ferguson, John N. ..... St. Paul
Ferguson, Richard H. ..... Rochester
Fernandez, Rafael F., Jr. ..... Minneapolis
£ Ferris, Deward O. ..... Rochester
Fesenmaier, Otto B. ..... Los Angeles, CA
† Fesler, Harold H. ..... W. St. Paul
Fetzek, Albert D. ..... Minneapolis
Feuling, John C. ..... Sun City, AZ
£ Fibuch, Eugene E. ..... Rochester
Field, Charles W. ..... Hopkins
Fifer, Ellen Z. ..... St. Paul
Fifer, William R. ..... Minneapolis

Fifield, Malcolm M. ..... Duluth
£ Filbuch, Eugene E. ..... Rochester
Filiatrault, L. J. ..... Coon Rapids
Filipovich, Orest N. ..... Minneapolis
Fingerman, David L. ..... Minneapolis
Fink, Daniel L. ..... St. Paul
Fink, Lawrence H. ..... Silver Spring, MD
† Fink, Leo W. ..... Minneapolis
£ Fink, Richard A. ..... Rochester
Fink, Robert J. ..... Minneapolis
Finkelnburg, William O. ..... Winona
Finkelstein, Joel ..... Rochester
Finlayson, Richard E. ..... Minneapolis
Finstad, James E. ..... Minneapolis
£ Fischer, Albert P. ..... Wayzata
Fischer, Robert F. ..... St. Paul
Fish, Charles R. ..... Rochester
Fisher, Don H. ..... Minneapolis
Fisher, Howard W. ..... Minneapolis
Fisher, Isadore I. ..... Minneapolis
Fisketti, Henry ..... Duluth
Fitch, Charles G. ..... Worthington
Fitzsimons, William E. ..... Brainerd
£ Fitzgerald, Robert H. ..... Rochester
£ Fitzgerald, Robert H., Jr. ..... Rochester
† Flancher, Leon H. ..... Detroit Lakes
Flanigan, Donald J. ..... Pensacola, FL
Flannery, Hubert F. ..... St. Paul
Fleming, Dean S. ..... Minneapolis
Flick, William F. ..... Cheyenne, WY
Fliehr, Richard R. ..... Minneapolis
Flinn, James B. ..... Redwood Falls
Floersch, Adrian J. ..... Owatonna
Flom, Reynold P. ..... St. Paul
Flom, Robert S. ..... St. Paul
Flora, George C. ..... Minneapolis
Florine, Martin C. ..... Madison Lake
Flory, William D. ..... Minneapolis
Fluegel, John O. ..... Minneapolis
Flynn, Bernard F. ..... Hibbing
Flynn, Louis L., Jr. ..... St. Paul
Foderick, John W. ..... Hastings
Foderick, Peter P. ..... Ada
Fogelberg, Emil J. ..... St. Paul
Foker, Leslie W. ..... Minneapolis
Foley, Robert R. ..... Minneapolis
Foley, William A. ..... Minneapolis
Folsom, Louis B. ..... Minneapolis
Foni, Iancu F. ..... Faribault
Fontana, Robert S. ..... Rochester
Forbes, Edward F. ..... Minneapolis
*† Ford, Burton C. ..... Marshall
£ Fordyce, Richard A. ..... Rochester
Foreman, Richard T. ..... St. Paul
Forsythe, James R. ..... St. Paul
Fortier, George M. A. ..... Little Falls
Fortier, George M. A., Jr. ..... Little Falls
Fortier, Rene G. ..... Mankato
Fortuny, Ignacio E. ..... Minneapolis
Foss, Donald L. ..... Minneapolis
† Foss, Edward L. ..... Condon, MT
Foster, Orley W. ..... Minneapolis
£ Foster, Thomas N., III ..... Rochester
Foulk, William T., Jr. ..... Rochester
Fowler, Franklin, Jr. ..... APO San Francisco, CA
Fox, James Rogers ..... Minneapolis
Fox, LeRoy J. ..... St. Paul
Fraley, Elwin E. ..... Minneapolis
† Franchere, Frederick W. ..... Lake Crystal
Francis, David W. ..... Morristown
Frane, Donald B. ..... Minneapolis
Frane, Gerald T. ..... Minneapolis
Franklin, Gordon W. ..... Northome
£ Fraser, Richard A. ..... Rochester
† Frederickson, Alice C. ..... Willmar
Frederickson, David L. ..... Duluth
Fredlund, Jon S. ..... Anoka
£ Freedman, Harvey M. ..... Rochester
Freeman, Charles D., Jr. ..... St. Paul
Freeman, Craig W. ..... Minneapolis
Freeman, Donald H. ..... Minneapolis
Freeman, Donald W. ..... St. Louis Park
£ Freeman, Richard E. ..... Rochester
French, Bayard T. ..... Hibbing
French, Lyle A. ..... Minneapolis
£ Freshman, John R. ..... Rochester
Frethem, Allen A. ..... Rochester
Frey, Richard J. ..... Minneapolis
Friberg, Joseph B. ..... Minneapolis
† Fricke, Robert E. ..... Rochester
Fried, Louis A. ..... Minneapolis
† Friedell, Aaron ..... Minneapolis
Friedell, George ..... Minneapolis
Friedlieb, Oskar P. ..... Virginia
Friedman, Harry S. ..... Minneapolis
Friedrich, Bradford E. ..... Red Wing
Friend, Charles A. ..... Minneapolis
† Fritsche, Albert ..... New Ulm
Fritsche, Carl J. ..... New Ulm
Fritsche, Theodore R. ..... New Ulm
Fritz, Wallace L. ..... St. Paul
† Froats, Charles W. ..... St. Paul
Frost, John B. ..... Minneapolis
Frost, John W. ..... St. Paul
Fruchtman, Stanley A. ..... Minneapolis
Frye, Charles W. ..... St. Paul
Frys, Russell N. ..... Minneapolis
£ Frytak, Stephen ..... Rochester
Fuglestad, Edson V. ..... Minneapolis
Fuglestad, J. Roald ..... Minneapolis
† Fuller, Alice H. ..... Minneapolis
Fuller, Benjamin F. ..... White Bear Lake
Fuller, Josiah ..... Duluth
† Funk, Victor K. ..... Hopkins
Funke, Joyce L. ..... St. Paul
Furlow, William L. ..... Rochester
Furman, L. Christine ..... Minneapolis
Furr, Leo ..... Bird Island

G

Gaard, Richard C. ..... Robbinsdale
Gaebe, Milton B. ..... Clara City
Gaertner, Frank M. J., Jr. ..... St. Paul
Gaertner, John R. ..... St. Paul
Gage, James R. ..... Minneapolis
Gaida, Joseph B. ..... St. Cloud

Gailitis, Veronika M. ....St. Paul
Galbraith, Richard F. ....Minneapolis
Galejs, Aina ....St. Paul
Gallagher, Larry J. ....Mound
Gallett, Lester E. ....Minneapolis
Galligan, John J. ....St. Paul
† Galligan, Margaret Mary D. ....Minneapolis
Galloway, Jackson R. ....Alexandria, LA
Galway, Charles F. ....St. Paul
† Gambill, Carl M. ....Rochester
† Gambill, Earl E. ....Rochester
Gamble, Elbert J. ....Roseville
Gamble, William G. ....Minneapolis
Gamm, Edgar R. ....Park Rapids
Gannon, Paul G. ....Minneapolis
Garamella, Joseph J. ....Minneapolis
Garber, George L. ....Winona
Garber, James J. ....Rochester
£ Gard, Joseph R. ....Rochester
Gardner, Jack K. ....Fairmont
* Gardner, Victor H. ....Fairmont
Gardner, Walter P. ....St. Paul
Garetz, Floyd K. ....Minneapolis
Garrick, James G. ....Bethesda, MD
† Garrow, Douglas M. ....St. Paul
Garske, George L. ....Minneapolis
Garten, Joseph L. ....Minneapolis
Garvey, James T. ....Minneapolis
Gasik, Joseph M. ....Minneapolis
Gastineau, Clifford F. ....Rochester
Gaute, Svend T. ....St. Paul
Gaviser, David ....Minneapolis
Gedgaudas, Eugene ....Minneapolis
Gedge, Stafford W. ....Rochester
† Gehlen, Joseph N. ....St. Paul
Geib, Marvin J. ....Fargo, ND
Geis, LeRoy F. ....Minneapolis
Geiser, Peter M. ....Alexandria
Geist, Robert W. ....St. Paul
Geller, Joseph ....Minneapolis
Gendron, Joseph L. ....St. Paul
Gentling, Peter A. ....APO San Francisco, CA
Gentry, William C., Jr. ....Minneapolis
George, Vane P., Jr. ....LeSueur
Geraci, Joseph E. ....Rochester
Gerend, Thomas J. ....Virginia
Gerstenkorn, George B. ....Milaca
Gerster, Paul W. ....Anoka
Gesundheit, Sim ....Minneapolis
Geurs, Benjamin R. ....Mankato
£ Ghosh, Manas K. ....Rochester
† Ghostley, Mary C. ....Bemidji
Gibbs, Edward C. ....St. Paul
£ Gibbs, Marvin K. ....Rochester
Gibbs, Robert W. ....Minneapolis
Giebenhain, John N. ....Minneapolis
† Giere, Joseph C. ....Minneapolis
† Giere, Richard W. ....Minneapolis
† Giere, Silas W. ....Benson
£ Gifford, William A. ....Rochester
Gilbert, Maurice G. ....Minneapolis
Gilbertsen, A. Sigrid ....Minneapolis
Gilbertsen, Victor A. ....Minneapolis
Gilchrist, Milton R. ....St. Paul
Gildersleeve, John W. ....Ft. Sam Houston, TX
Gill, Theodore M. ....Albert Lea
Gilles, Paul J. ....Minneapolis
Gilles, Thomas F. ....Fairfax
Gillespie, Delmar R. ....St. Paul
£ Gillespie, Donald N. ....Rochester
† Gillespie, Malcolm G. ....Duluth
Gilman, Lloyd C. ....Willmar
£ Gilsanz, Vicente ....Rochester
Gilsdorf, Donald A. ....St. Paul
† Gingold, Benjamin A. ....Minneapolis
Gislason, Paul H. ....Mankato
£ Gismondi, Pedro A. ....Rochester
Gisvold, John J. ....Rochester
Gjerde, William P. ....Lake City
Glaeser, John H. ....Minneapolis
Glenny, William R. ....St. Paul
Glick, Dallas D. ....Mountain Lake
Glomstad, Gary B. ....Grand Rapids
† Goblirsch, Andrew P. ....Wayzata
Godfrey, H. Wilson ....Minneapolis
Goehl, Reinhold O. ....Minneapolis
Goehrs, Gilman H. ....St. Cloud
£ Goellner, John R. ....Rochester
Goetz, Frederick C. ....Minneapolis
Gokcen, Barbara W. ....Minneapolis
Gokcen, Muharrem ....Minneapolis
† Goldberg, Isadore M. ....Minneapolis
Goldberg, Marvin E. ....Minneapolis
Goldberg, Robert J. ....St. Paul
Goldberg, Stanley M. ....Minneapolis
Goldfarb, Benjie L. ....Minneapolis
Goldfarb, Mace G. ....Minneapolis
Goldish, Daniel R. ....Duluth
Goldish, Robert J. ....Duluth
† Goldman, Theodore I. ....Minneapolis
Goldner, Meyer Z. ....Minneapolis
Goldschmidt, Volker ....Duluth
Goldsmith, Joseph W. ....St. Paul
Goldstein, Alan L. ....Hopkins
Goldstein, Norman P. ....Rochester
£ Goldyne, Marc E. ....Rochester
Goldston, Edgar C. ....Rochester
Goltz, Robert W. ....Minneapolis
Gonzales, Neva M. ....St. Cloud
£ Good, Andrew E. ....Rochester
Good, C. Allen, Jr. ....Rochester
Good, Gary ....Minneapolis
Good, Roy H. ....Northfield
Goodchild, William R. ....Minneapolis
Goodale, Robert L., Jr. ....Minneapolis
Goodall, David C. ....Deer River
Goodman, Ernest ....St. Paul
Goodnow, William H. ....Duluth
Goott, Bernard ....St. Paul
Gordon, A. Marc ....International Falls
Gordon, John R. ....Minneapolis
Gordon, Sewell S. ....Minneapolis
Gorman, Columba A. ....Rochester
Gould, Allan B., Jr. ....Rochester
£ Gould, Barry K. ....Rochester
Gould, Ronauld J. ....Anchorage, AL
Gowan, Lawrence R. ....Duluth
Gowan, Lawrence R., Jr. ....Duluth
Gower, Walter E. ....Duluth
Gozum, Ekrem ....Minneapolis
Grabow, Jack D. ....Rochester
Grados, Carlos ....Coon Rapids
Graf, John A. ....Rochester
Grage, Theodor B. ....Minneapolis
Graham, Asa B. ....Faribault
Graham, John J. ....Minneapolis
Grahek, Jack P. ....Ely
Grande, David W. ....Mankato

Granquist, Richard D. ....Minneapolis
Grant, James B. ....Minneapolis
Grant, John C. ....Sauk Centre
Grant, Suzanne ....Minneapolis
† Gratzek, Frank R. ....Anoka
Gravett, Desmond C. ....Rochester
† Gray, Royal C. ....Minneapolis
Greden, John F. ....Ft. Lee, VA
Green, Clayton R. ....Excelsior
Green, John F. ....Alexander
Green, Paul A. ....Rochester
Green, Robert A. ....Minneapolis
Greenberg, Albert J. ....Minneapolis
Greene, Gordon ....Hibbing
Greene, Laurence F. ....Rochester
Greene, Leonard H. ....Minneapolis
Greenfield, Theodore ....Champlin
Greenfield, Irving ....Minneapolis
Gregoire, Earl ....Bemidji
£ Greipp, Philip R. ....Rochester
¶ Greisheimer, Esther M. ....Philadelphia, PA
Gretsch, Gerald A. ....St. Paul
£ Greydanus, Donald E. ....Rochester
Gridley, John W. ....St. Paul
Griebie, Grant L. ....Hutchinson
Griffin, John W. ....Bemidji
Griffin, Patrick J. ....St. Paul
Griffin, Richard P. ....Benson
* Griffin, Thomas M. ....St. Paul
Griffiths, Robert W. ....El Paso, TX
Grimes, Burton P. ....St. Peter
Grimes, Marian ....Minneapolis
Grimes, Paul T. ....Park Rapids
Grimmell, Francis J. ....Minncapolis
Grinley, Andrew V. ....Grand Rapids
† Grinvalds, Anna O. ....Cambridge
£ Grismer, Jerome T. ....Wauwatosa, WI
Grohs, William H. ....Duluth
Gronquist, Y. K. J. ....Cloquet
Groover, Robert Vann ....Rochester
Grose, Frederick N. ....Clarissa
£ Gross, Earl C. ....Rochester
Gross, John B. ....Rochester
Grossling-Freudenburg, Sergio ....Rochester
Grossling, Higinia ....Minneapolis
Grubbs, Larry T. ....Rochester
Grube, David W. ....Minneapolis
Gruys, Robert I. ....Minneapolis
Gudio, Felix A., Jr. ....St. Paul
Gruninger, Robert P. ....St. Paul
Guerrero, Rafael A. ....Minneapolis
Guilfoile, Pierre J. ....Delano
£ Guller, Barbara ....Rochester
Gullickson, Glenn, Jr. ....Minneapolis
Gumnit, Robert J. ....St. Paul
Gunlaugson, Frederick G. ....Minneapolis
£ Gura, George M., Jr. ....Rochester
Gustafson, Paul O. ....Minneapolis
Gustafson, Robert W. ....Granite Falls
Gustason, Harold T. ....Minneapolis
Gustilo, Ramon B. ....Minneapolis
Guthrie, J. Cameron ....St. Paul
Gutzmann, Bruce W. ....Faribault
Guy, Jack A. ....New London

H

£ Haakenson, Robert C. ....Rochester
Haas, Jack F. ....Northfield
Haas, John W. ....Minneapolis
Haase, Donald D. ....Silver Bay
Haavik, John E. ....Duluth
£ Habein, Harold C. ....Palo Alto, CA
* Haberer, Helen R. ....Stacy
Haberle, Charles A. ....Minneapolis
£ Haddad, Paul G. ....Rochester
† Haes, Julius E. ....St. Peter
Haesly, Warren W. ....Winona
Hagberg, Norman L. ....Montevideo
Hagedorn, Albert B. ....Rochester
Hagen, John D. ....Austin
Hagen, Kristofer ....Minneapolis
Hagen, Wayne S. ....Minneapolis
Haglin, John J. ....Minneapolis
Hahn, Richard G. ....Rochester
† Haines, Samuel F. ....Rochester
Hakanson, Erick Y. ....St. Paul
Hakim, Ali A. ....Minneapolis
Halbert, John J. ....Duluth
† Halenbeck, Philip L. ....St. Cloud
Hall, Arthur M. ....Minneapolis
Hall, Barnard ....St. Paul
Hall, Harry B. ....Minneapolis
Hall, Loren J. ....Minneapolis
Hall, Wendell H. ....Minneapolis
† Hallberg, Olav Erik ....Rochester
Hallgren, Roger ....Belle Plaine
Halliday, Phillip V. ....Duluth
Hallin, Roger P. ....Worthington
† Halloran, Walter H. ....Jackson
Halme, William B. ....Wadena
Halper, Bernard ....Hibbing
Halpern, David J. ....Brewster
Halverson, Kermit J. ....Parkville
Halverson, William G. ....Madelia
Halvorsen, Daniel K. ....Owatonna
Halvorson, David C. ....Northfield
Halvorson, Harold C. ....Albert Lea
Halvorson, James W. ....Zumbrota
Hambidge, Gove, Jr. ....Minneapolis
Hamel, Arnold L. ....Minneapolis
Hamel, Joseph I. ....Minneapolis
Hammar, Lawrence M. ....Mankato
Hammerstrom, Robert N. ....Minneapolis
Hammes, Ernest M., Jr. ....St. Paul
£ Hancock, William E. ....Rochester
Handler, Seymour ....Minneapolis
Hanisch, Edward C., Jr. ....Minneapolis
Hanlon, David G. ....Rochester
Hannon, Donald W. ....St. Paul
* Hanover, Ralph D. ....International Falls
† Hansen, Cyrus O. ....Minneapolis
† Hansen, Erling W. ....Minnetonka
Hansen, Milo L. ....Little Falls
† Hansen, Olga S. ....Minneapolis
Hansen, Robert E. ....Hibbing
Hansen, Rollin M. ....Minneapolis
Hansen, Theodore M. ....Albert Lea

Hanske, Edward A. ..... Minneapolis
Hanson, A. Stuart ..... Minneapolis
Hanson, Ernest O. ..... Cloquet
† Hanson, Harlow J. ..... Minneapolis
Hanson, Harold B. ..... Burnsville
Hanson, Harold W. ..... Minneapolis
*† Hanson, Henry V. ..... Green River, AZ
Hanson, Lewis ..... Frost
*† Hanson, Malcolm B. ..... Osseo
Hanson, Mark C. L. ..... Minneapolis
£ Hanson, Norman P. ..... Rochester
Hanson, Mildred S. ..... Minneapolis
Hanson, Norbert O. ..... Rochester
§ Hanson, Mark T. ..... Faribault
Hanson, Stephen L. ..... Minneapolis
† Hanson, William A. H. ..... Minnetonka
Hanson, William B. ..... Minneapolis
Hanton, Edward M. ..... St. Paul
Harbaugh, John T. ..... St. Cloud
£ Harder, Edward J. ..... Rochester
† Hargraves, Malcolm M. ..... Rochester
Harkness, John W. ..... Minneapolis
Harmon, Gaius E. ..... St. Paul
Harper, David G. ..... Duluth
† Harrington, Stuart W. ..... Rochester
Harrington, Vernon A. ..... Duluth
Harris, John E. ..... Minneapolis
Harris, Leon D. ..... Minneapolis
Harris, Max E. ..... St. Paul
Harrison, Percy W. ..... Worthington
Harrison, William C. ..... Minneapolis
Hart, Terril H. ..... Wayzata
† Hart, William E. ..... Monticello
† Hartfiel, William F. ..... St. Paul
Hartfield, James E., Jr. ..... Rochester
Hartig, Marjorie ..... St. Paul
Hartig, Paul R. ..... Minneapolis
Hartman, Evelyn E. ..... Minneapolis
¶ Hartmann, Ronald J. ..... Rochester
Hartnagel, Grant F. ..... Red Wing
Hartung, Elmer H. ..... Claremont
Hartwich, Roger F. ..... Winona
Hartwig, John A. ..... Minneapolis
Harty, Jerome L. ..... Minneapolis
Hartzell, Allan J. ..... Duluth
Hartzler, Paul L. ..... Cambridge
Harvey, Clyde B. ..... Minneapolis
Hass, Frederick M. ..... Minneapolis
Hastings, Donald W. ..... Minneapolis
Hauge, Erling T. ..... Minneapolis
† Hauge, Malvin I. ..... Marcell
Haugen, George W. ..... Minneapolis
Haugen, John A. ..... Minneapolis
Haus, Erhard ..... St. Paul
Hauser, Charles W. ..... St. Paul
Hauser, Donald C. ..... Minneapolis
† Hauser, Victor P. ..... St. Paul
Havel, Robert J. ..... Minneapolis
Haven, Walter K. ..... Minneapolis
Havig, Terrance A. ..... Lubbock, TX
Hawk, Dale J. ..... St. Charles
Hawkinson, Harlan W. ..... St. Paul
† Hawkinson, Raymond P. ..... Minneapolis
Hawley, George M. B., II ..... Red Wing
Hay, Lyle J. ..... Minneapolis
Hayashi, Melvin M. K. W. ..... Rochester
Hayes, Albert F. ..... St. Paul
Hayles, Alvin B. ..... Rochester
Hays, Albert T. ..... Minneapolis
Haywa, E. William ..... Minneapolis
Hazen, Richard W. ..... Willmar
† Head, Douglas P. ..... Minneapolis
Heagle, C. Russell ..... Waconia
Hebbel, Robert ..... Minneapolis
† Hebeisen, Milton B. ..... Chaska
† Heck, Frank J. ..... Rochester
† Heck, William W. ..... St. Paul
Hedemark, Homer H. ..... Ortonville
† Hedemark, Truman A. ..... Ortonville
Hedenstrom, Charles W. ..... St. Paul
† Hedenstrom, Frank G. ..... St. Paul
Hedenstrom, Philip C. ..... Marshall
Hedenstrom, Richard H. ..... St. Paul
† Hedlund, Charles J. ..... St. Paul
Hedrick, William L. ..... Minneapolis
Heegaard, William G. ..... Alexandria
Hegrenes, Robert L. ..... Hutchinson
Hegstad, Thomas C. ..... Windom
† Heiam, William C. ..... Cook
Heiberg, Olaf M. ..... Worthington
Heid, James K. ..... Little Falls
† Heidel, Werner ..... Cresskill, NJ
Heimark, John J. ..... Mankato
Heimel, Albert J. ..... St. Paul
£ Heinberg, Charles E. ..... Rochester
Heinz, Ivy B. ..... Shakopee
Heinz, John N. ..... Minneapolis
Heinzerling, Carl R. ..... Chaska
Heise, Carl vR ..... Winona
Heise, Herbert vR ..... Winona
Heise, Paul vR ..... Winona
Heise, William vR ..... Winona
Heisel, John G. ..... Duluth
£ Heithoff, Kenneth B. ..... Richfield
Held, William J. ..... St. Cloud
Helgaas, Steffen A. ..... Farmington
£ Helgason, Pall B. ..... Rochester
Heller, Ben I. ..... Mankato
Heller, Edgar E. ..... Mankato
Heller, Steven A. ..... Minneapolis
Helmholz, Henry F., Jr. ..... Rochester
† Helseth, Hovald K. ..... Fergus Falls
Helwig, Karl L. ..... Virginia
Hempel, Dean J. ..... Minneapolis
Henderson, Edward D. ..... Rochester
Henderson, John W. ..... Rochester
Henderson, Lowell L. ..... Rochester
Henderson, Terrance P. ..... White Bear Lake
Hendricks, John L. ..... Rochester
£ Hendrickson, Ronald R. ..... Rochester
† Hengstler, William H. ..... St. Paul
Henke, Clarence Earl ..... Rochester
Henke, Wilbert J. ..... St. Paul
Henrikson, Earl C. ..... Minneapolis
† Henry, Clarence J. ..... Onamia
Henry, Harold W. ..... Moose Lake
Henry, James S. ..... St. Paul
Henry, John C. ..... Owatonna
Henry, Joseph E. ..... Milaca
Henry, Kenneth G. ..... Owatonna
Hensley, Manuel ..... St. Paul
Hepper, Norman G. ..... Rochester
Herber, Leo ..... Thief River Falls
† Herbert, Willis L. ..... Minneapolis
Hergott, Patrick F. ..... Waseca
Herland, Alexander L. ..... Winona
† Herman, Samuel M. ..... Fort Lauderdale, FL

Hermans, Paul E. ..... Rochester
Herrick, Donald W. ..... St. Paul
† Hertel, Garfield E. ..... McAllen, TX
Hesla, Inman A. ..... Austin
Hess, Carroll N. ..... Minneapolis
† Hetzler, John A. ..... White Bear Lake
Heupel, Hermann W. ..... Minneapolis
† Hewitt, Edith S. ..... Rochester
Hewitt, Marshall I. ..... Minneapolis
Hiatt, John A. ..... Minneapolis
Hickok, David F. ..... Minneapolis
Hick, John F. ..... Winona
Hiduchenko, Katherine ..... Minneapolis
Hildebrand, John E. ..... Bemidji
Hildebrandt, Walter C. ..... Minneapolis
Hilding, Anderson C. ..... Duluth
Hildreth, Thomas A. ..... San Francisco, CA
Hilgedick, William R. ..... Minneapolis
Hilger, Jerome A. ..... St. Paul
Hilger, Laurence D. ..... St. Paul
Hilgers, Robert D. ..... St. Paul
Hilgermann, George O. ..... Minneapolis
Hilker, Marcus D. ..... St. Paul
Hilker, Robert T. ..... Owatonna
Hill, Charlotte W. ..... St. Paul
Hill, David L. ..... Minneapolis
Hill, Earl ..... Minneapolis
Hill, Elmer M. ..... Minneapolis
Hill, John R. ..... Rochester
Hill, Richard W. ..... Rochester
Hiller, Bruce H. ..... Minneapolis
Hinckley, Robert G. ..... White Bear Lake
Hinderaker, Harris P. ..... Willmar
Hines, Edgar A., Jr. ..... Brevard, NC
† Hiniker, Louis P. ..... St. Paul
† Hiniker, Peter J. ..... St. Peter
Hinz, Walter E. ..... Willmar
Hippchen, Ray C. ..... St. Paul
Hirsh, Stanton A. ..... Crookston
Hitchcock, Claude R. ..... Minneapolis
Ho, Shu Kang ..... St. Paul
Hoagland, H. Clark ..... Rochester
Hobday, H. Thomas ..... St. Cloud
Hodapp, Robert V. ..... Willmar
Hodges, Kenneth V. ..... Minneapolis
¶ Hodgins, Carol L. ..... Rochester
Hodgson, Corrin H. ..... St. Paul
Hodgson, Jane E. ..... St. Paul
Hodgson, John R. ..... Rochester
£ Hodgson, Stephen F. ..... Duluth
Hoeg, Dwight C. ..... Duluth
† Hoeper, Philip G. ..... Chestnut Hill, MA
Hoff, Herbert O. ..... Duluth
Hoffert, Henry E. ..... Minneapolis
Hoffman, Neil R. ..... Minneapolis
† Hoffman, Roy A. ..... Minneapolis
Hoffman, Walter Lees ..... Minneapolis
Hofmann, Gerald N. ..... Minneapolis
£ Hogan, William M. ..... Rochester
Hoganson, Donald E. ..... Bemidji
Hohmann, Albert ..... St. Paul
Holbrook, Margaret A. ..... Rochester
† Holcomb, Joel T. ..... Marine-on-the-St. Croix
Holland, C. R. ..... Rochester
Hollenhorst, Robert W. ..... Rochester
Hollinshead, W. H. ..... St. Paul
Holm, Donald F. ..... Minneapolis
Holm, Owen W. ..... Hibbing
Holman, Colin B. ..... Rochester
Holmberg, Conrad J. ..... Minneapolis
Holmstrom, Carle H. ..... Warren
Holt, Glen E. ..... Duluth
† Holt, John E. ..... St. Paul
Holten, John ..... Moorhead
Holzapfel, Fred C. ..... Minneapolis
Hom, Leong Y. W. ..... Fergus Falls
Honath, Donald H. ..... Owatonna
Hood, Roderick P. ..... Duluth
Hoover, Norman W. ..... Chicago, IL
Hopkins, G. Wendell ..... Minneapolis
Hopperstad, J. Jerome ..... Minneapolis
Hoppes, Emerson E. ..... Minneapolis
Horecki, Henry ..... Minneapolis
Horns, Howard L. ..... Minneapolis
Horns, Norman ..... Minneapolis
Horns, Richard C. ..... Minneapolis
Horowitz, Arthur J. ..... Minneapolis
£ Horswill, Robert N. ..... Rochester
† Horton, Bayard T. ..... Rochester
Hoseth, Wayne L. ..... Minneapolis
Hottinger, George C. ..... St. Paul
Hottinger, Raymond C. ..... Janesville
Houglum, Arvid J. ..... Duluth
† Houkom, Bjarne ..... Fergus Falls
† Houkom, S. Sverre ..... Duluth
Houle, Rollin J. ..... New Brighton
Houlton, William H. ..... St. Paul
House, James H. ..... Minneapolis
Householder, James R. ..... Minneapolis
Houser, Otis ..... Rochester
Houts, Joseph C. ..... Dassel
Hovde, Gordon W. ..... Lindstrom
Hovland, Melvin L. ..... Minneapolis
Hovland, Richard D. ..... Minneapolis
Howard, David ..... Long Prairie
Howard, Frank M., Jr. ..... Rochester
£ Howard, John D. ..... Rochester
£ Howard, Richard J. ..... Edina
Howard, Robert B. ..... Minneapolis
Howard, Solomon E. ..... Minneapolis
Howe, Newell W. ..... West St. Paul
Howell, Carter W. ..... Minneapolis
Howell, John L. ..... Minneapolis
Howell, Llewelyn P. ..... Rochester
Hoyt, C. Sherman ..... Minneapolis
Hruza, William J. ..... Sioux Falls, SD
£ Hu, Chung-Hong ..... Rochester
Huber, Robert W. ..... St. Croix Falls, WI
Hubin, Edwin G. ..... Sandstone
£ Hudson, Albert W. ..... Rochester
Huebert, Dan W. ..... Hutchinson
£ Huerta, Enrique ..... Rochester
Huff, John S. ..... Minneapolis
Huffington, Herb L. ..... Waterville
† Huffington, Herbert L. ..... Brownsville, TX
Hughes, Bernard J. ..... St. Cloud
Hughes, Sidney O. ..... Winona
Hulteng, Donald B. ..... Minneapolis
Hunt, Arthur B. ..... Carmel, CA
Hunt, James C. ..... Rochester
Hunt, Kai K. ..... Alexandria
¶ Hunt, Max L. ..... Rochester
Hunt, Vincent R. ..... Minneapolis
Hung, Jui-Sung ..... Minneapolis
Hunter, Murray H. ..... Farmington
Hunter, Samuel W. ..... St. Paul
Hurr, Maland C. ..... Minneapolis
Hurwitz, Milton M. ..... St. Paul

Huseby, Thomas L. ..... St. Paul
Husebye, Kjeld O. ..... St. Paul
Hustad, Edward G. ..... Minneapolis
£ Huston, Kent A. ..... Rochester
† Hutchinson, Henry ..... Brainerd
Hymes, Alan C. ..... Minneapolis
† Hymes, Charles ..... Minneapolis
£ Hynes, Kieran M. ..... Rochester

I

Ibrahim, George W. ..... Virginia
Ide, Arthur W., Jr. ..... Minneapolis
Idstrom, Linneus G. ..... Minneapolis
Indeck, Walter ..... Minneapolis
Ingalls, Edgar G. ..... Minneapolis
£ Ireland, Damian C. R. ..... Rochester
† Ireland, Gerald W. ..... St. Paul
£ Irons, G. Benton ..... Rochester
Isaacson, Ronald ..... Mathers AFB, CA
Isele, Reginald H. ..... Austin
£ Ivance, Richard J. ..... Rochester
Iverslie, Philip C. ..... Minneapolis
Iverson, Eleanor B. ..... Minneapolis
Iverson, Paul C. ..... Grand Rapids
Iverson, Rolf M. ..... Minneapolis
Ivins, John C. ..... Rochester

J

Jackish, George E. ..... Red Wing
Jacklin, Alexander J. ..... Duluth
† Jackman, Raymond J. ..... Rochester
£ Jackman, Steven ..... Rochester
£ Jackson, Charles B. ..... Rochester
Jackson, J. Albert ..... Minneapolis
Jackson, Richard L. ..... Minneapolis
Jackson, William C. ..... St. Paul
Jacobs, Douglas L. ..... Willmar
† Jacobson, Clarence ..... Chisholm
Jacobson, Clifford W. ..... Breckenridge
Jacobson, Dennis ..... Onamia
Jacobson, Ferdinand C. ..... Duluth
Jacobson, Leslie W. ..... Minneapolis
Jacobson, Loren J. ..... Minneapolis
Jacoby, John S. ..... Minneapolis
Jacobson, Wyman E. ..... Minneapolis
Jacott, William E. ..... Duluth
Jaeger, Dwight E. ..... St. Cloud
Jaffe, Manuel O. ..... Minneapolis
James, Ellery M. ..... St. Paul
James, John W. ..... St. Paul
£ James, Reese E. ..... Rochester
Janda, George W. ..... Minneapolis
Janda, Wayne E. ..... Austin, TX
£ Jander, Hartwig P. ..... Rochester
Janecek, James, Jr. ..... St. Paul
Janecky, Allen G. ..... Baudette
Janes, Joseph M. ..... Rochester
Janssen, Martin E. ..... St. Paul
Jarvis, Charles W. ..... St. Paul
Jarvis, Mary B. ..... Minneapolis
Jastram, Rupert M. ..... St. Paul
Jay, Alan R. ..... Temple, TX
Jefferies, William L. ..... Minneapolis
Jensen, Alvin M. ..... Brownton
Jensen, Nathan K. ..... Minneapolis
Jensen, Paul A. ..... Minneapolis
Jensen, Reynold A. ..... Minneapolis
Jenson, James E. ..... Stillwater
Jepson, William W. ..... Minneapolis
Jerome, Bourne ..... Minneapolis
Jerome, Elizabeth B. K. ..... Minneapolis
Jeronimus, Henry J. ..... Duluth
* Jessico, Charles M. ..... Duluth
Jeub, Robert P. ..... Minneapolis
£ Jilek, Dennis D. ..... Rochester
John, Byron L. ..... St. Cloud
Johnson, Alan R. ..... Windom
Johnson, Aldridge F. ..... St. Paul
Johnson, Angelo G. ..... Minneapolis
Johnson, Arthur B. ..... Minneapolis
Johnson, Bradley D. ..... Minneapolis
Johnson, Calvin J. ..... Grand Rapids
Johnson, Carl Edwin ..... St. Paul
Johnson, Carl Eric ..... Rochester
Johnson, Carolyn A. ..... St. Paul
† Johnson, C. Percy ..... Tyler
Johnson, Curtis A. ..... Princeton
Johnson, Curtis M. ..... Winona
Johnson, Daniel A. ..... Litchfield
Johnson, Daniel T. ..... St. Paul
Johnson, David R. ..... Minneapolis
Johnson, Donald A. ..... Minneapolis
Johnson, Douglas L. ..... Brainerd
Johnson, Edward A. ..... Minneapolis
† Johnson, Einer W. ..... Bemidji
Johnson, Einer W., Jr. ..... Rochester
Johnson, Frank E. ..... Minneapolis
Johnson, Franklin L. ..... Duluth
Johnson, Gordon E. ..... Minneapolis
Johnson, Harry A., Jr. ..... Minneapolis
Johnson, Herbert W. ..... St. Paul
† Johnson, James A. ..... Minneapolis
Johnson, John W. ..... Minneapolis
Johnson, Karl E. ..... Duluth
Johnson, Lyle O. ..... St. Paul
£ Johnson, Marvin W. ..... Rochester
† Johnson, Norman P. ..... Minneapolis
Johnson, Norman Paul ..... St. Paul
† Johnson, Norton T. ..... Minneapolis
Johnson, O. Guy ..... St. Paul
† Johnson, Olga H. ..... Detroit Lakes
Johnson, Paul E. ..... Wayzata

* Johnson, Ralph B. ..... Lanesboro
Johnson, Reinald G. ..... Minneapolis
Johnson, Rex R. ..... New Ulm
Johnson, Richard J. ..... St. Paul
Johnson, Richard S. ..... Minneapolis
Johnson, Richard V. ..... Minneapolis
Johnson, Robert E. ..... Minneapolis
Johnson, Robert H. ..... St. Paul
Johnson, Roger L. ..... St. Paul
Johnson, Theodore L. ..... Duluth
Johnson, Thomas E. ..... St. Paul
£ Johnson, Thomas F. ..... Orlando, FL
Johnson, Thomas H., Jr. ..... Minneapolis
Johnson, Vilhelm M. ..... Dawson
£ Johnson, Warren L., Jr. ..... Rochester
Johnson, William E. ..... St. Cloud
Johnson, William J. ..... Rochester
Johnson, Youbert T. ..... Minneapolis
Johnsrud, Luverne W. ..... Hibbing
Johnston, Bemis H. ..... Eatontown, NJ
Johnston, Donald K. ..... Minneapolis
Johnston, H. Wayne ..... Virginia
Johnston, Leonard F. ..... Winona
Jones, David G. ..... Minneapolis
£ Jones, H. Royden, Jr. ..... Rochester
† Jones, Herbert W., Jr. ..... Minneapolis
£ Jones, Ian V. ..... Rochester
† Jones, Orville H. ..... Mankato
Jones, Richard H. ..... Minneapolis
† Jones, Richard N. ..... St. Cloud
Joransen, James A. ..... Minneapolis
Jordan, Donald V. ..... Minneapolis
£ Jordan, James J. ..... Rochester
¶ Jordan, Kathleen B. Smith ..... Granite Falls
Jorgensen, Edward O. ..... Rochester
Jorgensen, Donald R. ..... St. Paul
Jorgensen, Harlan ..... Minneapolis
Joseph, Arnold H. ..... St. Paul
Joyce, John W. ..... Rochester
Judd, Allen S. ..... Minneapolis
Judd, Edward S. ..... Rochester
Judd, Walter H. ..... Washington, D.C.
† Juergens, Herman M. ..... Belle Plaine
Juergens, Manley F. ..... Stillwater
Juers, Edward H. ..... Red Wing
£ Juncos, Louis I. ..... Rochester
Juntunen, Roy R. ..... Duluth
† Jurdy, Mitchell ..... Minneapolis
† Just, Herman J. ..... Hastings

K

Kaczrowski, William M. ..... Marshall
Kadesky, Harold B. ..... Minneapolis
Kaese, Werner E. ..... Rochester
£ Kahler, John G. ..... Minneapolis
£ Kaine, Richard F. ..... Rochester
Kaiser, Harold B. ..... Minneapolis
Kaiser, Milton L. ..... New Ulm
Kalb, Thomas J. ..... Minneapolis
† Kallestad, Leonard L. ..... Minneapolis
Kaminski, Gregory W. ..... Redwood Falls
Kane, Dennis J. ..... Minneapolis
Kane, Morton C. ..... Minneapolis
Kane, William J. ..... Minneapolis
Kanne, Earl R. ..... Brainerd
Kantar, Yale C. ..... St. Paul
Kaplan, Arnold P. ..... Minneapolis
Kaplan, David H. ..... Edina
Kaplan, J. Jacob ..... Minneapolis
Kaplan, Martin B. ..... Minneapolis
£ Kaplan, Roy A. ..... Rochester
Karges, Laurel E. ..... Grand Rapids
Karish, Louis J. ..... Grand Rapids
Karleen, Conrad I. ..... Minneapolis
Karlen, Markle ..... Minneapolis
Karn, Jacob F. ..... Ortonville
Karnes, William E. ..... Rochester
Karon, Everett H. ..... St. Paul
Karon, Irvine M. ..... St. Paul
† Kasper, Eugene M. ..... St. Paul
Kasper, Robert E. ..... Minneapolis
† Kath, Reinhard H. ..... Merrifield
Katkov, Harold ..... Minneapolis
Katz, Beni ..... Minneapolis
Katz, Elliott S. ..... Phoenix, AZ
Katz, Harry I. ..... Minneapolis
Katz, Louis J. ..... Long Beach, CA
Kaufman, Edward J. ..... Appleton
*† Kaufman, William C. ..... Appleton
Kaye, Dale R. ..... Minneapolis
Kazmier, Francis J. ..... Rochester
Kearney, R. Wynn ..... Mankato
† Kearney, R. Wynn, Jr. ..... Rochester
Kearns, Thomas P. ..... Rochester
Keenan, Thomas P. ..... St. Paul
Kegel, James F. ..... Minneapolis
Keil, Marcus A. ..... Albert Lea
† Keith, Haddow M. ..... Rochester
† Keith, Norman M. ..... Rochester
Keith, Paul J. ..... Milaca
Keithahn, Elmer E. ..... Sleepy Eye
Kelalis, Panayotis P. ..... Rochester
† Kelby, Gjert M. ..... Minneapolis
Kelley, Roger E. ..... Crosby
Kelly, Edward H. ..... St. Paul
Kelly, Helen M. ..... West St. Paul
Kelly, James H. ..... St. Cloud
Kelly, John C. ..... Minneapolis
Kelly, John F. ..... Cold Spring
Kelly, John P. ..... Minneapolis
£ Kelly, John T. ..... Minneapolis
Kelly, Joseph R. ..... St. Paul
Kelly, Patrick J. ..... Rochester
Kelly, Robert T. ..... Grand Rapids
Kelly, William D. ..... Minneapolis
£ Kelman, Donald B. ..... Rochester
† Kelsey, Carleton G. ..... St. Paul
Kelsey, Chauncey M. ..... St. Paul
† Kemp, Alphonse F. ..... Mankato
*† Kenefick, Emmett V. ..... St. Paul
Kennedy, Byrl J. ..... Minneapolis
Kennedy, Charles C. ..... Rochester
† Kennedy, Claude C. ..... Minneapolis

† Kennedy, George L. ..... Faribault
Kennel, Arthur J. ..... Kinshasa, Congo
Kenyon, Thomas J. ..... St. Paul
£ Kepfer, Percy D. ..... Rochester
† Kernohan, James W. ..... Rochester
Kerr, Frederick W. L. ..... Rochester
† Kesting, Herman ..... St. Paul
Kevern, Jay L. ..... Henning
£ Key, Samuel N., III ..... Rochester
Keyes, Robert W. ..... Pipestone
Khorsand, Darius ..... Minneapolis
Kieffer, Stephen A. ..... Minneapolis
Kiely, Joseph M. ..... Rochester
Kierland, Robert R. ..... Rochester
Kiesler, Frank ..... Grand Rapids
† Kilbride, Edwin A. ..... Worthington
Kilen, Mark B. ..... Duluth
£ Killean, James E. ..... Rochester
£ Kim, Hyun-Hahk ..... Rochester
Kim, Kyoung ..... Worthington
Kim, Mark K. ..... St. Paul
Kimmel, George C. ..... Minneapolis
Kimmel, George E. ..... Rochester
Kincaid, Owings W. ..... Rochester
Kind, Allan C. ..... Minneapolis
† King, Frances W. ..... Minnetonka
King, John E. ..... Ft. Worth, TX
Kinkade, Byron R. ..... Ada
Kinney, William N. ..... Anoka
Kiolbasa, Edward B. ..... Stillwater
£ Kipfer, Robert E. ..... Rochester
† Kippen, Neil ..... Breckenridge
Kirby, Thomas J., Jr. ..... Rochester
Kirklin, John W. ..... Birmingham, AL
Kiser, Joseph C. ..... Minneapolis
Kitzberger, Peter J. ..... New Ulm
Kjellsen, Douglas L. ..... Minneapolis
Klass, Donald W. ..... Rochester
KLC—Mikusciak, George M. ..... Belle Plaine
Klefstad, Lloyd H. ..... Greenbush
† Klein, Harry ..... Duluth
Kleinkauf, Thomas P. ..... Hutchinson
Kleinsasser, Warren L. ..... St. Paul
Kleven, Lowell H. ..... Minneapolis
Kluge, John W. ..... St. Paul
Knapp, James F. ..... Detroit Lakes
Knapp, Miland E. ..... Minneapolis
† Knight, Ralph T. ..... Minneapolis
† Knight, Ray R. ..... Minneapolis
Knip, Robert J. ..... Ortonville
Knipp, William J. ..... Brainerd
Knobloch, William H. ..... Minneapolis
Knoche, Harvey A. ..... Gaylord
Knoedler, John P. ..... Duluth
† Knoll, W. V. ..... Brainerd
Knowles, Richard A. ..... Minneapolis
Knowles, Roy C. ..... St. Paul
Knowles, William D. ..... Mankato
Knudsen, Helen L. ..... Minneapolis
Knutson, Gerhard E. ..... St. Paul
Knutson, Lewis A. ..... Spring Grove
Knutson, Robert C. ..... St. Paul
£ Kobayashi, Itsuro ..... Rochester
Kodres, Nina ..... St. Paul
Koelz, Thomas A. ..... St. Paul
Koenig, Robert P. ..... St. Cloud
Kohlhase, Robert E. ..... Minneapolis
Kohls, Gary G. ..... Milaca
Kolars, Charles P. ..... Minneapolis
† Kolars, James J. ..... Faribault
† Koller, Hermann M. ..... Minneapolis
*† Koller, Louis R. ..... Minneapolis
Koller, Robert L. ..... Minneapolis
Kollmorgen, Rodger C. ..... West Point, NY
£ Kondo, Kiyotaro ..... Rochester
Konicek, Robert G. ..... Rochester
Kooda, Jennings C. ..... Morris
Koons, William R. ..... Mahnomen
Koontz, Peter S. ..... Minneapolis
Koop, Severin H., Jr. ..... St. Cloud
Koos, Gerald W. ..... Minneapolis
£ Koppers, Lawrence E. ..... Rochester
£ Koretzky, Emil ..... Rochester
Korchik, John P. ..... Minneapolis
Korda, Henry A. ..... Pelican Rapids
Koropchak, Nikolai ..... Minneapolis
¶ Kortz, Louise S. ..... Rochester
Kosiak, Michael ..... St. Paul
Kosiak, William ..... St. Paul
Koskela, L. E. ..... Moose Lake
Kostich, Nikola D. ..... Minneapolis
† Kostick, William R. ..... Fertile
† Kotchevar, Frank R. ..... Sun City, CA
Kottke, Frederic J. ..... Minneapolis
Kotval, Russell J. ..... Pipestone
† Koucky, Rudolph W. ..... Sagle, ID
Kovack, Freeman D. ..... Minneapolis
Koza, Donald W. ..... St. Paul
Kozak, Michael J. ..... Minneapolis
Kozel, William J. ..... Morris
Kraemer, George N. ..... Fairmont
Krafft, Walter E. ..... Minneapolis
Kragh, Lyle V. ..... Minneapolis
Kramer, Daniel W. ..... Minneapolis
Kramer, James D. ..... St. Paul
Krause, Carl W. ..... Fairmont
Kremen, Arnold J. ..... Minneapolis
Kremer, Jerome L. ..... Montevideo
† Kreuzer, Titus C. ..... New Brighton
Krezowski, Thomas K. ..... St. Paul
Krieser, Albert E. ..... Minneapolis
Kreiser, Robert D. ..... Fergus Falls
Krigsten, Eli J. ..... Weisbaden, Germany
£ Krohn, John R. ..... Rochester
Krupp, Neal E. ..... Rochester
Kruzich, Stephen J. ..... St. Cloud
Krystosek, Lee A. ..... Minneapolis
Kubista, Theodore P. ..... San Diego, CA
† Kucera, Frank J. ..... Hopkins
Kucera, Stanley T. ..... Northfield
† Kucera, William J. ..... Santa Barbara, CA
Kuehner, Marvin E. ..... Red Wing
£ Kuers, Peter F. W. ..... Rochester
£ Kuge, Mark T. ..... Rochester
Kugler, Alex A. ..... St. Paul
£ Kuglitsch, Jack F. ..... Rochester
Kuhlmann, Lawrence B. ..... Melrose
Kuhlmann, Vernon G. ..... Alexandria
£ Kulak, Linton L. ..... Rochester
Kulstad, Oscar S. ..... Dodge Center
* Kulzer, Norbert J. ..... Hastings
Kump, Warren L. ..... Minneapolis
Kundel, Donald W. ..... Duluth
£ Kunert, Raoul T. ..... Rochester
Kuske, Albert W. ..... St. Paul
Kuslich, Stephen ..... Minneapolis

Kusske, Bradley W. ..... St. Paul
Kusske, Douglas R. ..... St. Paul
Kussy, James C. ..... Little Falls
Kusz, Clarence V. ..... Minneapolis
Kuz, Eugene L. ..... Savage
Kvale, James N. ..... Shakopee
Kvale, John ..... Long Prairie
Kvam, Lowell L. ..... St. Paul
Kvamme, Brynjulv ..... Mabel
Kvistberg, Gerald K. ..... St. Cloud
Kwako, Jerome E. ..... Duluth
Kyle, Robert A. ..... Rochester
Kyllo, John E. ..... Minneapolis
Kyllonen, Ronald R. ..... Minneapolis

L

L'Abbe, A. J. Philip ..... Duluth
L'Heureux, Philippe R. ..... Minneapolis
LaBree, John W. ..... Minneapolis
LaBree, Robert H. ..... Duluth
Lackore, Leonard K. ..... Willmar
Lade, Roswith I. ..... St. Paul
LaFave, James W. ..... St. Paul
£ LaFlamme, Georges-Henri ..... Rochester
LaFond, Edward M. ..... St. Cloud
Lagaard, Sheldon ..... Minneapolis
Laikola, Leslie A. ..... Adrian
† Lajoie, John M. ..... Minneapolis
Lake, Clifford F. ..... Rochester
Lamb, H. Douglas ..... Minneapolis
Lampert, Ronald M. ..... St. Paul
Lamusga, David J. ..... Minnetonka
Landsman, Gordon S. ..... Minneapolis
Lane, Jerald P. ..... Minneapolis
Lane, Miles I. ..... White Bear Lake
Lang, Leonard A. ..... Minneapolis
Langer, Leonard O., Jr. ..... Minneapolis
Langseth, Rodney N. ..... Duluth
£ Lanier, Anne P. ..... Rochester
£ Lanier, James F. ..... Rochester
Lannin, Bernard G. ..... St. Paul
Lannin, Donald R. ..... St. Paul
Lannon, James B. ..... Minneapolis
† Lapierre, Arthur P. ..... Minneapolis
Larkin, John E. ..... St. Paul
Larrabee, Walter F., Jr. ..... Willmar
Larsen, Frank W. ..... Minneapolis
£ Larsen, Russell H. ..... Burnsville
Larson, Allen K. ..... Minneapolis
Larson, Arthur K. ..... Minneapolis
Larson, Carol Ann ..... Minneapolis
Larson, Donald Marvin ..... Duluth
Larson, Donald Myren ..... Minneapolis
Larson, Donald R. ..... Crosby
Larson, Dorette W. ..... Fergus Falls
Larson, Ernest J., Jr. ..... Minneapolis
Larson, Eva Jane O. ..... St. Paul
Larson, F. Wilmer ..... Minneapolis
Larson, Gerald E. ..... Cambridge
Larson, Jerrold V. ..... St. Paul
Larson, Kenneth R. ..... Moose Lake
Larson, Lawrence M. ..... Minneapolis
Larson, Leighton W. ..... Waconia
† Larson, Leroy J. ..... Bagley
Larson, Loren J. ..... Minneapolis
† Larson, Milo H. ..... St. Peter
Larson, Oliver E. H. ..... Zumbrota
Larson, Richard E. ..... Minneapolis
Larson, Roger C. ..... Minneapolis
Larson, Theodore G. ..... Brainerd
Larson, Wyllis G. ..... Minneapolis
Larter, Roland R. ..... Hallock
† Laszewski, Franz von Zelberschwecht ..... St. Paul
Latterell, Kenneth E. ..... Duluth
Latts, Elliot M. ..... Minneapolis
Lauritzen, Herbert ..... Minneapolis
Lavender, Dick R. ..... St. Louis Park
£ Laventman, Jaime ..... Rochester
† LaVake, Rae T. ..... Minneapolis
Law, Harrison E. ..... Viriginia
Lawler, Kevin M. ..... St. Paul
£ Lawrence, Robert B. ..... Rochester
Lawrence, Van S. ..... Minneapolis
Lawrow, John W. ..... Minneapolis
Lawson, Warren R. ..... Minneapolis
Lawton, James J., Jr. ..... Minneapolis
Laxdal, Stefan D. ..... Minneapolis
Layman, Thomas E. ..... St. Paul
Layer, James M. ..... Minneapolis
£ Lazar, Anthony S. ..... Rochester
† Leach, Clifford G. ..... St. Paul
Leach, Thomas C. ..... Babbitt
Leahy, Dennis M. ..... St. Paul
Leary, Frank J. ..... Rochester
Leavelle, Dennis E. ..... San Antonio, TX
Leavenworth, Richard O., Jr. ..... Minneapolis
† Leck, Paul C. ..... Palm Desert, CA
Lee, Gordon E. ..... Glenwood
Lee, Hubert W. ..... Brainerd
Lee, Ju Hao ..... Minneapolis
Lee, Norman J. ..... Tracy
Lee, Raymond A. ..... Rochester
Lee, Robert E. ..... Rochester
Lee, William C. ..... Hibbing
Leek, Joseph H. ..... Duluth
Leemhuis, Andrew J. ..... Minneapolis
Lees, David C. ..... Minneapolis
Lees, Jack R. ..... St. Paul
Lehman, Donald S. ..... St. Paul
Lehmann, James D. ..... Waconia
Lehrer, Alfred J., Jr. ..... Montgomery
Leick, Richard M. ..... St. Paul
Leiferman, Robert J. ..... Minneapolis
Leighton, John S. ..... Minneapolis
Leih, George G. ..... Virginia
Leino, Walter B., Jr. ..... Ely
Leinonen, Wendla E. ..... Anoka
£ Leist, Frederick D. ..... Rochester
† Leitch, Archibald ..... South St. Paul
Lelwica, Thaddeus J. ..... Staples
† Lenander, Mellvin E. L. ..... St. Peter
Lenarz, Albert J. ..... St. Cloud
Lenz, Bernard W. ..... Minneapolis
Lenz, Joseph R. ..... Morton

Lenz, Oa ..... Minneapolis
Leonard, Paul F. ..... Rochester
Leonard, Samuel ..... Minneapolis
Leonard, Stanley A. ..... St. Paul
Leonardson, Peter Y. ..... Silver Bay
† Leopard, Brand A. ..... Brownsville, TX
Leppink, Harold B. ..... Two Harbors
Leppo, N. Erkki A. ..... Duluth
Lerdahl, Kenneth ..... St. Paul
Lerner, A. Ross ..... Minneapolis
Lerner, Irving J. ..... St. Paul
Leslie, Loren R. ..... Minneapolis
Leslie, W. Robert ..... Minneapolis
Lessard, Richard J. ..... St. Paul
Lester, John W. ..... Mapleton
Lester, Malcom J., Jr. ..... Truman
Lester, Theodore H. ..... Minneapolis
Letson, Robert D. ..... Minneapolis
Leven, N. Logan ..... St. Paul
Leverenz, Carleton W. ..... St. Paul
Levine, Howard M. ..... Minneapolis
Levine, Norman D. ..... Minneapolis
Levitan, Leonard H. ..... St. Paul
Levitt, George X. ..... St. Paul
Levitt, Seymour H. ..... Minneapolis
† Levy, Jonathan M. ..... Rochester
Levy, Michael ..... Minneapolis
Lewis, Charles W. ..... Henning
Lewis, F. Bruce ..... Minneapolis
Lewis, Glenn M., Jr. ..... Minneapolis
Lewis, Joyce S., Jr. ..... St. Paul
Lick Louis C. ..... Minneapolis
Lick, William J. ..... St. Paul
Liebhaber, Henia F. ..... Anoka
Lien, Richard J. ..... St. Paul
† Lightbourn, Edgar L. ..... Hastings
Lilleberg, Norbert J. ..... St. Paul
Lillehei, James P. ..... Minneapolis
Lillehei, Richard C. ..... Minneapolis
Lillie, Andrew R. ..... St. Paul
Lillie, John C. ..... Rochester
Lima, Ludvig R. ..... Montevideo
Limbeck, Donald A. ..... Minneapolis
Lin, Hong-Chien ..... Waconia
¶ Lind, Judy E. ..... Rochester
Lindahl, Merlyn J. ..... Sherburn
Lindall, Arnold W., Jr. ..... Marine-on-St. Croix
Lindberg, Evan F. ..... Minneapolis
Lindberg, Vernon L. ..... Minneapolis
Lindberg, Winston R. ..... Minneapolis
Lindblom, Alton E. ..... North Mankato
Lindeland, Arthur T. ..... Minneapolis
Lindell, Robert E. ..... St. Paul
Lindeman, Raymond J. ..... Paynesville
Lindemann, Charles E. ..... Minneapolis
Linderholm, Bruce E. ..... Minneapolis
Lindgren, Russell C. ..... Minneapolis
Lindquist, Dale C. ..... Lindstrom
Lindquist, Max F. ..... South St. Paul
Lindsay, Malcolm I., Jr. ..... Rochester
Lindseth, Esten ..... Excelsior
Linman, James W. ..... Rochester
Linnell, Leonard S. ..... Duluth
Linner, John H. ..... Minneapolis
Linner, Paul W. ..... Minneapolis
£ Lippman, Harry H. ..... Rochester
* Lippman, Hyman S. ..... St. Paul
* Lipmann, Elmer W. ..... Hutchinson
Lipschultz, Oscar ..... Minneapolis
† Litin, Edward M. ..... Hopkins
Litkewitsch, Helene ..... St. Paul
Litman, Abraham B. ..... Minneapolis
† Litman, Samuel N. ..... Duluth
Litman, Thomas ..... St. Louis Park
£ Little, John R. ..... Rochester
£ Litwak, Oscar ..... Rochester
Litzow, Thaddeus J. ..... Rochester
Lobell, Michael ..... St. Paul
Lober, Paul H. ..... Minneapolis
Locke, Murray S. ..... Minneapolis
£ Lockwood, Reed R. ..... Rochester
Loeb, George L. ..... St. Cloud
Loes, Louis A. ..... St. Cloud
Lofgren, Eric P. ..... Rochester
Lofgren, Karl A. ..... Rochester
Lofsness, Stanley V. ..... Minneapolis
Lofstrom, Dennis E. ..... Brainerd
Logan, George B. ..... Rochester
£ Logan, William S. ..... Rochester
Lohmann, John G. ..... Pipestone
Loken, Merle K. ..... Minneapolis
Loken, Selmer M. ..... St. Paul
Loken, Theodore ..... Ada
Lommen, Morris ..... Austin
Lommen, Peter A., Jr. ..... Austin
Long, Donlin M. ..... Minneapolis
Long, John C. ..... Chicopee Falls, MA
Longfellow, Helen W. ..... Brainerd
£ Longstreth, George F. ..... Rochester
Loos, Gerald D. ..... APO, New York, NY
Lorentzen, Ernest S. ..... Detroit Lakes
Lott, Frederick H. ..... Minneapolis
† Love, J. Grafton ..... Rochester
† Lovett, Beatrice R. ..... Minnetonka
Lowe, Alexander D. ..... South St. Paul
Lowe, Douglass A. ..... Minneapolis
† Lowe, Thomas A. ..... South St. Paul
Lowry, Jeanette K. ..... Minneapolis
Lowry, Paul T. ..... Minneapolis
Lu, Cheng-en ..... Fergus Falls
Lu, Jennie W. G. ..... Fergus Falls
Luby, Thomas H. ..... St. Cloud
Lucas, Alexander R. ..... Rochester
£ Lucas, Charles T. ..... Rochester
† Luck, Hilda ..... Mankato
Luckey, William T. ..... Minneapolis
Ludes, Bernard F. ..... Rochester
Lueck, Wallace W. ..... Minneapolis
Lueders, James H. ..... Evansville
Lufkin, Murray W. ..... St. Paul
† Lufkin, Nathaniel H. ..... Minneapolis
Luh, Edwin F. ..... Fergus Falls
Lukinac, Charles J. ..... Minneapolis
Lukk, Olaf ..... Prior Lake
Lund, George W. ..... Minneapolis
Lund, J. Benjamin ..... Mankato
Lund, Nancy R. ..... Minneapolis
£ Lund, Richard E. ..... Rochester
Lund, Richard R. ..... Minneapolis
† Lund, Werner J. ..... Staples
Lundblad, Rodger R. ..... Minneapolis
*† Lundblad, Roy A. ..... Minneapolis
Lundblad, Stanley W. ..... Minneapolis
† Lundeberg, Karl R. ..... Minneapolis
Lundell, Carl L. ..... Granite Falls
† Lundholm, Arthur M. ..... Princeton
Lundquist, Charles B. ..... Minneapolis
Lundquist, Curt W. ..... Owatonna
Lundquist, Virgil J. ..... Minneapolis

Lundsten, Leslie C. ..... Bemidji
Lunzer, Richard G. ..... St. Paul
Lynch, Francis W. ..... St. Paul
Lynch, Michael F. ..... Minneapolis
Lynch, Raymond P. ..... St. Paul
Lynch, Richard P. ..... St. Paul
† Lynde, Orrin G. ..... Los Gatos, CA
Lynn, Hugh B. ..... Rochester
Lyon, Fred A. ..... Minneapolis
Lyon, John D. ..... Hopkins
Lyons, John R. ..... St. Cloud
Lysne, Richard B. ..... Minneapolis
Lysyj, Anatol ..... Minneapolis
Lyzenga, Anton G. ..... Minneapolis

M

McAfee, David K. ..... Willmar
McBean, James B. ..... Rochester
McBride, Alexander M. ..... Mankato
McBride, John W. ..... St. Paul
£ McBurney, P. Louis ..... Rochester
McCafferty, Charles ..... St. Paul
McCaffrey, F. John ..... Minneapolis
McCain, Donovan L. ..... St. Paul
McCampbell, Malcolm D. ..... Minneapolis
£ McCann, William D. ..... Rochester
McCannel, Malcolm A. ..... Minneapolis
McCarten, Francis M. ..... Stillwater
McCarthy, Austin M. ..... Willmar
McCarthy, Charles J. ..... St. Paul
† McCarthy, Donald ..... Minneapolis
McClellan, Robert J. ..... St. Paul
McClelland, John G. ..... Virginia
McCloud, C. Naumann ..... St. Paul
McCollister, Robert J. ..... Minneapolis
McConahey, William M., Jr. ..... Rochester
McCormick, Donald P. ..... Minneapolis
£ McCoy, Stephen H. ..... Rochester
† McDaniel, Orianna ..... Minneapolis
† McDaniel, Samuel P. ..... Lakeville
£ McDonald, Thomas J. ..... Rochester
£ McDougall, John C. ..... Rochester
† McDowell, John P. ..... St. Cloud
£ McDuffie, Richard W., Jr. ..... Rochester
£ McElfresh, Edward C. ..... Rochester
McEllistrem, Edward J. ..... St. Paul
McEllistrem, Gerald D. ..... St. Paul
McEnaney, James E. ..... Owatonna
McEwan, Alexander ..... St. Paul
† McFarland, Arthur H. ..... Minneapolis
† McGandy, Robert F. ..... Minneapolis
McGee, Hugh E., Jr. ..... Fort Lee, GA
McGill, Douglas B. ..... Rochester
McGovern, Lawrence O. ..... Minneapolis
McGroarty, Brian J. ..... St. Paul
McHutchison, Samuel K. ..... North St. Paul
McIlrath, Donald C. ..... Rochester
£ McIlroy, Gary T. ..... Rochester
† McInerny, Maurice W. ..... Minneapolis
£ McIntyre, Donald G. ..... Rochester
† McIntyre, John A. ..... Owatonna
† McKelvey, John L. ..... St. Paul
McKelvey, John M. ..... Minneapolis
McKenna, Charles H. ..... Rochester
McKenna, James L. ..... Minneapolis
McKenna, John J. ..... Virginia
† McKenna, Jay K. ..... LaJolla, CA
McKenna, Maurice J. ..... Grand Rapids
McKenzie, Charles H. ..... Minneapolis
McKenzie, Eva E. ..... St. Paul
McKhann, Charles F. ..... Minneapolis
McKinlay, Gordon L. ..... Minneapolis
McKinley, C. Richard ..... Minneapolis
† McKinney, Frank S. ..... Minneapolis
† McLane, William O. ..... Brainerd
McLaughlin, Byron H. ..... Minneapolis
McMahon, John E. ..... Minneapolis
£ McMullan, Mart ..... Rochester
McNamara, John P. ..... Rice
McNeil, John J. ..... Minneapolis
McNeil, Maurice R. ..... Glencoe
McNeil, John A. ..... St. Paul
† McNutt, John R. ..... Duluth
McParland, Felix A., Jr. ..... Minneapolis
*† McPheeters, Herman O. ..... Minneapolis
McQuoid, David W. ..... Excelsior
¶ McShane, Sister M. Quentin ..... Rochester
£ MacCarty, Collin S. ..... Rochester
£ MacCarty, Robert L. ..... Rochester
£ MacCarty, William C., III ..... Rochester
MacCornack, Robert L., Jr. ..... South St. Paul
† MacDade, Albert D. W. ..... Rochester
MacDonald, Charles J. ..... Rochester
† MacDonald, Daniel A. ..... Minneapolis
MacDonald, Roger A. ..... Grand Marais
† MacDonald, Vance D. ..... Rochester
MacGibbon, James D. ..... Minneapolis
MacKinnon, Donald C. ..... Minneapolis
† Macklin, William E., Jr. ..... Litchfield
MacLean, Alexander R. ..... Rochester
† MacRae, Gordon C. ..... Duluth
† Mach, Frank B. ..... Minneapolis
Mach, John R. ..... Minneapolis
Mach, Ralph F. ..... Pine City
Macheledt, Neil L. ..... Anoka
† Macklin, William E. ..... Litchfield
Mackoff, Samuel ..... Phoenix, AZ
Madland, Robert S. ..... St. Paul
Madsen, Donald O. ..... Minneapolis..
Maeder, Edward C. ..... Minneapolis
Maeder, Edward C., Jr. ..... Minneapolis
† Magath, Thomas B. ..... Rochester
Magee, Timothy M. ..... Minneapolis
Magid, Gail A. ..... Santa Cruz, CA
† Magney, Fredolph H. ..... Duluth
Magnuson, Raymond C. ..... Combridge
Mahan, Charles S. ..... Minneapolis
Maher, Frank T. ..... Rochester
Mahle, Donald G. ..... Wabasha
£ Maish, George O., Jr. ..... Rochester
Maitland, Edwin T. ..... Willmar
£ Malagelada, Juan R. ..... Rochester
† Malek, Reza S. ..... Rochester
Malerich, J. Anthony ..... Cottage Grove
Malkasian, George D. ..... Rochester
Malmquist, Carl P. ..... Minneapolis
Malone, Patrick M. ..... Willmar

Mandel, Sheldon L. ..... Minneapolis
£ Manesis, John G. ..... Rochester
Manick, Kenneth P. ..... Minneapolis
Mankey, James C. ..... Minneapolis
Mankin, Harold T. ..... Rochester
Manlove, Charles H., Jr. ..... St. Paul
Mann, George A. ..... Minneapolis
Manoles, Elias N. ..... Minneapolis
Manolis, Deane C. ..... Minneapolis
£ Manson, Roberto R. ..... Rochester
£ Mantel, Fred ..... Hopkins
Marcia, Alfred ..... Anoka
Marcoux, J. Paul ..... Rochester
Marion, Dennis F. ..... Wright AFB, OH
£ Marik, Francis ..... Rochester
Mark, Aaron L. ..... Minneapolis
Mark, Merle S. ..... Minneapolis
Mark, Peter M. ..... Minneapolis
Marking, George H. ..... Minneapolis
Markland, Colin ..... Minneapolis
Markovitz, Jack M. ..... Minneapolis
£ Marmer, Robert H. ..... Rochester
Marshall, Clark M. ..... Crosby
Marshall, John F. ..... Pine Island
£ Marsiglia, Juan C. ..... Rochester
Marso, John L. ..... Mankato
Marta, John B. ..... St. Paul
Martalock, Dean L. ..... Great Lakes, IL
Marte, Egon ..... Minneapolis
Martens, Theodore G. ..... Rochester
£ Martimbeau, Pierre ..... Rochester
Martin, Doreen A. ..... Pepin, WI
Martin, Dwight L. ..... St. Paul
Martin, Frank E. ..... Minneapolis
Martin, Frederick F. ..... Bagley
Martin, George B. ..... Thief River Falls
Martin, George R. ..... Minneapolis
Martin, Gordon M. ..... Rochester
Martin, Harold R. ..... Rochester
¶ Martin, James E. ..... Rochester
Martin, John T. ..... Rochester
Martin, Maurice J. ..... Rochester
£ Martin, Raymond A. ..... Rochester
Martin, Webster C. ..... Duluth
Martinson, Carl J. ..... Wayzata
Martinson, Elmer J. ..... Wayzata
Martinson, Raymond M. ..... Virginia
Marvin, Joseph E. ..... Brainerd
Maryland, Daniel L. ..... Duluth
Maslansky, Robert A. ..... Minneapolis
Massee, Joseph S. ..... Minneapolis
£ Masserman, Richard L. ..... Rochester
† Masson, Duncan M. ..... Rochester
† Masson, James C. ..... Rochester
Masson, James K. ..... Rochester
Mast, Frederic L. ..... Chisholm
Mastbaum, Leonard T. ..... Minneapolis
Mateo, Guillermo ..... St. Paul
Mathers, John E. ..... Duluth
Mathews, Wallace E. ..... Mankato
† Mathieson, Don R. ..... Rochester
Mathison, Larry A. ..... Fergus Falls
£ Mathison, Robert D. ..... Rochester
£ Matlak, Michael E. ..... Rochester
Matson, Roland W. ..... Spring Valley
* Matthews, James H. ..... Minneapolis
Matthews, John A. G. ..... Minneapolis
† Mattison, Percy A. ..... Winona
Mattson, Donald S. ..... Willmar
Mattson, Roger A. ..... Minneapolis
Matus, Richard N. ..... St. Paul
Maunder, John B. ..... Minneapolis
Maus, Donald J. ..... Monticello
Maus, Philip W. ..... Dawson
† Maxeiner, Stanley R. ..... Minneapolis
Maxeiner, S. R., Jr. ..... Minneapolis
May, Horst G. ..... Duluth
May, Robert B. ..... St. Cloud
Mayberg, Donald M. ..... Minneapolis
Mayne, John G. ..... Rochester
Mazzitello, William F. ..... St. Paul
Meany, Thomas J. ..... Minneapolis
Mears, Burtis J. ..... St. Paul
Mecklenburg, Fred E. ..... Minneapolis
Medelman, John P. ..... St. Paul
Medina, Ambrosio M., Jr. ..... Wayzata
Meeker, Henry C. ..... Minneapolis
Meekin, Patrick C. ..... Minneapolis
† Meinert, Albert E. ..... Winona
Meinert, John K. ..... Willmar
Melancon, Joseph F. ..... St. Paul
Melich, Paz C. ..... St. Paul
Melichar, Paul J. ..... Minneapolis
Meller, Maurice ..... Brainerd
Meller, Robert L. ..... Minneapolis
£ Mendelson, Bryan C. ..... Rochester
Mendesh, Anthony N. ..... Duluth
Mendiola, Ramon P., Jr. ..... Waconia
Menefee, Edward C. ..... Albert Lea
Mennis, William I. ..... Staples
Mensheha, Nicholas M. ..... Minneapolis
Mercil, William F. ..... Crookston
Meredith, Donald C. ..... Mankato
Merner, Thomas B. ..... Minneapolis
† Merrick, Charlotte T. ..... St. Paul
Merrick, Robert L. ..... St. Paul
Merrick, William G. ..... Duluth
Merrill, Daniel C. ..... Minneapolis
Merrill, Robert ..... Des Moines, IA
Merritt, Wallace A. ..... Rochester
Mersy, David J. ..... Red Lake Falls
Messenheimer, Myron G. ..... Minneapolis
Messick, Joseph M., Jr. ..... Rochester
Metcalf, Norman ..... Princeton
£ Metter, Earl J. ..... Rochester
Metz, Donald D. ..... Minneapolis
Meyer, Alvin J. ..... Minneapolis
Meyer, Frederick C. ..... Kenyon
£ Meyer, James J. ..... Rochester
Meyer, Howard J. ..... Duluth
† Meyer, Paul F. ..... Faribault
Meyer, Richard H. ..... Faribault
Meyer, Robert P. ..... Faribault
Meyer, William C. ..... Rochester
Michael, Alfred F. ..... Minneapolis
*† Michael, Joseph C. ..... Pompano Beach, FL
Michaelis, Dorothy L. ..... Duluth
† Michel, Henry H. ..... Minneapolis
Michels, Roger P. ..... Willmar
† Michelson, Henry E. ..... Minneapolis
Michienzi, Leonard J. ..... St. Paul
† Mickelsen, Emma F. (Fronk) ..... Holmes Beach, FL
Mickelson, John C. ..... Los Angeles, CA
Midboe, Gilbert T. ..... Forest Lake
Middlebrook, John E. ..... Minneapolis
Midthune, Andreen S. ..... Lake Park
Midyett, F. Allan ..... Memphis, TN
Miettunen, John B. ..... Hibbing
Mijares, Wilfredo S. ..... Fairmont

Miks, George M. ....Aurora
† Milhaupt, Emmett N. ....Dunedin, FL
Miller, Albert G. ....St. Paul
Miller, Fletcher A. ....St. Paul
Miller, Gerald J. ....Ft. Riley, KS
Miller, H. Dawes ....Minneapolis
Miller, Harry G. ....Virginia
Miller, Harold E. ....Minneapolis
Miller, Herman ....Austin
Miller, Hugo E. ....Minneapolis
Miller, J. Carleton ....Minneapolis
Miller, Joe I., Jr. ....Rochester
Miller, Roland D. ....Rochester
Miller, Ross H. ....Rochester
Miller, W. Eugene ....Rochester
Miller, William P. ....Minneapolis
Miller, Winston R. ....St. Paul
Miller, Zondal R. ....St. Paul
Millett, D. Keith ....Minneapolis
Millikan, Clark H. ....Rochester
Mills, John L. ....Winnebago
Mills, Stephen D. ....Rochester
Milnar, Frank J. ....St. Paul
Milroy, Thomas W. ....Minneapolis
Minder, John G. ....Minneapolis
Mindrum, Gerald G. ....Minneapolis
Minge, Raymond K. ....Worthington
Minsky, Armen A. ....Minneapolis
Mintalar, Jose M. ....Winsted
Mishek, Charles J. ....St. Paul
Mitby, Irvin L. ....Minneapolis
Mitchell, Berton D. ....Minneapolis
† Mitchell, Edward C. ....College Place, WA
Mitchell, George S. ....St. Paul
Mitchell, John C., III ....Travis AFB, CA
Mitchell, Mancel T. ....Minneapolis
Mixer, Harry W. ....Minneapolis
£ Mizalis, Athanasios J. ....Rochester
Mlinar, Joseph P. ....Austin
Mock, Charles J. ....Virginia
Moe, John H. ....Minneapolis
† Moe, W. Wyatt ....Minneapolis
Moehn, John T. ....Minneapolis
† Moen, Johannes K. ....Minneapolis
† Moersch, Frederick P. ....Fort Lauderdale, FL
† Moersch, Herman J. ....Rochester
Moffitt, Emerson A. ....Rochester
£ Mokri, Bahram ....Rochester
Moghaddam, Alaeddin ....Minneapolis
† Molander, Herbert A. ....North St. Paul
Molenaar, Robert E. ....Cannon Falls
Moller, Julie C. ....Duluth
Moller, Jurgen ....West St. Paul
Molnar, George D. ....Rochester
Monahan, Robert H. ....St. Paul
Mongé, James J. ....Duluth
Monserud, Nels O. ....Cloquet
£ Monkman, George R. ....Rochester
Monson, Einer M. ....Minneapolis
Monson, Leonard J. ....Canby
Monson, Paul S. ....Mound
Monson, Warren A. ....Minneapolis
Montaniel, Necito L. ....Crookston
Montgomery, Guy E. ....Park Rapids
† Montgomery, Hamilton ....Rochester
Moody, David L. ....Minneapolis
Mooney, Robert D. ....St. Paul
£ Moore, Barry B. ....Rochester
Moore, Gordon L., II ....Rochester
† Moore, Irvin H. ....Eden Prairie
Moorhead, Marie ....Minneapolis
Moos, Daniel J. ....Minneapolis
Moral, Harvey M. ....Minneapolis
Moran, Leo J. ....New Brighton
Moran, Paul T. ....St. Cloud
† Morehead, Dewey E. ....Bodega Bay, CA
Moren, J. Adelaide ....St. Paul
Morgan, Hugh O. ....Amboy
Mori, Hideo ....Grand Meadow
Moriarty, Joseph A. ....Minneapolis
Moriarty, Joseph D. ....Coon Rapids
£ Morimoto, Allen M. ....Rochester
Mork, A. Harold ....Anoka
Mork, Frank E. ....Anoka
Mork, Frank E., Jr. ....Minneapolis
Mork, John N. ....Worthington
Morlock, Carl G. ....Rochester
£ Morrey, Bernard F. ....Rochester
Morrison, Robert R. ....Park Papids
Morrow, George W., Jr. ....Rochester
† Morse, Morton P. ....LeRoy
Morse, Robert M. ....Rochester
Morse, Roger D. ....LeRoy
*† Mortensen, Nels G. ....St. Paul
Mortenson, Howard O. ....Menahga
† Mosby, Maurice E. ....Long Prairie
Moss, Nyel H. ....Minneapolis
Mosser, Donn G. ....Minneapolis
Mossman, Philip L. ....Minneapolis
£ Motto, Joseph D. ....Rochester
Moulton, Keith B. ....St. James
Mouritsen, Glenn J. ....Fergus Falls
Mowlem, Albert ....St. Paul
Moyer, John B. ....Duluth
Moyer, Leonard B. ....Minneapolis
Moyer, Richard R. ....Hibbing
Muchow, Gene C. ....Austin
Mueller, Donald R. ....Grand Rapids
Mueller, Henry M. ....St. Paul
Mueller, James M. ....Minneapolis
Mueller, LeRoy E. ....Hendricks
Mueller, Rudolph B. ....Richmond
Muesing, Mark A. ....Tyler
Muesing, William J. ....New Ulm
Muhm, John R. ....Lawton, OK
£ Mulcahy, John J. ....Ann Arbor, MI
Mulder, Donald W. ....Rochester
Mulder, Richard D. ....Ivanhoe
Mulford, Beatrice ....St. Paul
Mulholland, William M. ....Minneapolis
£ Mullen, Bernard J. ....Rochester
Muller, A. Eugene ....North St. Paul
Muller, John J. ....Hibbing
Muller, Sigfrid A. ....Rochester
Mulligan, Arthur M. ....Brainerd
Mullin, Gerald T., Jr. ....Minneapolis
Mulrooney, John ....Winona
Mulvahill, John E. ....Minneapolis
Mundahl, Harold R. ....St. Paul
Munger, James E. ....Duluth
Munkittrick, Ronald C. ....Minneapolis
Munneke, Lyle ....Clara City
Munson, Martin S. ....Moose Lake
Murn, Thomas G. ....St. Cloud
Murphy, Jack T. ....St. Paul
† Murphy, Joseph W. ....Rochester
Murphy, Joseph E. ....Marshall
Murphy, Thomas R. ....Stillwater

† Murphy, William R. C. ..... Minneapolis
Murray, Charles L. ..... Minneapolis
Murray, Elisabeth M. ..... Minneapolis
Murray, Robert A. ..... Hibbing
Murray, Robert A., Jr. ..... St. Cloud
Musachio, Nicholas F. ..... St. Paul
Muschenheim, Frederick ..... Minneapolis
Muske, Marvin M. ..... Minneapolis
Mussey, Mary E. ..... Rochester
Musty, Nicholas J. ..... Minneapolis
Muus, John H. ..... Staple
Myaya, Po ..... St. Pau
Myers, Jay A. ..... Minneapoli
Myers, John W. ..... Canby
Myers, Theodore P. ..... Albert Lea
Myers, Thomas T., III ..... Minneapolis
Myhre, James A. ..... Minneapolis
Myhre, John H. ..... Fergus Falls
Mylrea, Murray J. ..... Burnsville
† Myre, Clifford R. ..... Paynesville

N

Nagobads, Ilgvars J. ..... Minneapolis
Nagobads, V. George ..... Minneapolis
Najarian, John S. ..... Minneapolis
Nakamura, James Y. ..... Detroit Lakes
Nash, Eldore B. ..... Minneapolis
Nathan, Fred F. ..... Ellsworth AFB, SD
£ Nauman, James C. ..... Rochester
* Nauth, Bernard S. ..... Edina
Navratil, Donald R. ..... Glencoe
† Neal, Joe M. ..... Minneapolis
Nealy, Donald E. ..... Adrian
Nealy, Timothy E. ..... Blooming Prairie
* Neary, Richard P. ..... Minneapolis
Neault, Roger W. ..... Rochester
Neel, Harry B. ..... Albert Lea
† Neel, H. Bryan, III ..... Rochester
Neel, Henry B. ..... Albert Lea
Neff, Walter S. ..... Virginia
Neher, Frederick J. ..... St. Paul
Nehring, John D. ..... Chaska
Neils, Vernon E. ..... St. Cloud
£ Neinas, Frederick W. ..... Rochester
Neira, Edward H. ..... St. Paul
Nelimark, Donald R. ..... Virginia
£ Nelson, Audrey M. ..... Rochester
Nelson, Bernette G. ..... Ely
£ Nelson, Bernice A. ..... New Brighton
Nelson, C. Barton ..... Minneapolis
Nelson, Carleton A. ..... Minneapolis
Nelson, Clayton E. J. ..... Albert Lea
£ Nelson, David J. ..... St. Paul
£ Nelson, David W. ..... Minneapolis
Nelson, Delbert R. ..... St. Paul
Nelson, Edward N. ..... Minneapolis
Nelson, Evan L., Jr. ..... Minneapolis
* Nelson, George E. ..... Minneapolis
Nelson, Glen D. ..... Minneapolis
Nelson, Glenn E. ..... Redwood Falls
Nelson, Gunard A. ..... Minneapolis
† Nelson, Harvey ..... Deerfield Beach, FL
† Nelson, Henry E. ..... Crookston
Nelson, John W. ..... Duluth
Nelson, Lloyd S. ..... Mineapolis
Nelson, Loren E. ..... St. Paul
Nelson, Louis A. ..... St. Paul
Nelson, Luther A. ..... Rush City
Nelson, Maxine O. ..... Minneapolis
Nelson, Maynard C. ..... Minneapolis
Nelson, O. L. Norman ..... Minneapolis
£ Nelson, Robert P. ..... St. Paul
Nelson, Ronald J. ..... St. Paul
Nelson, Roger L. ..... Rochester
Nelson, Ronald J. ..... St. Paul
Nelson, Roy A. ..... Fergus Falls
Nelson, Wallace I. ..... Minneapolis
Nerenberg, Sidney ..... Minneapolis
Neshiem, Martin O. ..... Albert Lea
Ness, Duane E. ..... Wadena
Ness, Richard A. ..... Fergus Falls
Nesse, Anton S. ..... Minneapolis
Nesse, James A. ..... Austin
Nesset, David G. ..... Rochester
Nesset, Lawren B. ..... Minneapolis
Nesset, William D. ..... Minneapolis
Nesvacil, Leon ..... St. Paul
Neumann, Roland F. ..... Minneapolis
Neumeister, Charles A. ..... Minneapolis
£ Neupert, Jerrol R. ..... Rochester
Neuwirth, Gerardo D. ..... Minneapolis
Niazi, Suad A. ..... Granite Falls
Nicholas, S. Scott, Jr. ..... Minneapolis
Nichols, Donald R. ..... Rochester
Nichols, Thomas O. ..... St. Paul
£ Nichols, Victoria R. ..... Rochester
Nicholson, Richard W. ..... Fergus Falls
Nickerson, John R. ..... Faribault
Nickerson, Neil D. ..... Fairmont
Nicolette, Charles C. ..... Minneapolis
£ Niedringhaus, Robert D. ..... Rochester
Nielsen, David J. ..... Minneapolis
Nietfeld, Aloys B. ..... Sauk Centre
£ Nijensohn, Daniel E. ..... Rochester
Nilsen, John A. ..... Minneapolis
£ Nimlos, Kenneth O. ..... St. Paul
£ Nimlos, Lenore O. ..... St. Paul
£ Nisbet, William ..... Rochester
Nisius, George F. ..... Duluth
£ Niven, Robert G. ..... Rochester
Nisswandt, Albert L. ..... Duluth
Nixon, James B. ..... Crosby
£ Nolan, Declan R. ..... Rochester
Nolan, Robert K. ..... Minneapolis
Nolan, William ..... Litchfield
Nollet, Donald J. ..... Hibbing
£ Noller, Kenneth L. ..... Rochester
Noran, Harold H. ..... Minneapolis
Noren, George R. ..... Minneapolis
† Norberg, Carl E. ..... Los Altos, CA
Norberg, William J. ..... Detroit Lakes
Nord, Robert E. ..... Minneapolis
Nordberg, Robert J. ..... Little Falls
† Nordlie, Paul E. ..... Minneapolis
Nordlund, Mildred E. ..... Carmichael, CA
Nordman, Willard F. ..... Mora
Noren, George R. ..... Minneapolis

Norman, David D. .....St. Paul
Norman, Franklin C. .....Minneapolis
Norman, Mark L., Jr. .....Minneapolis
Normann, Stephen T. .....Waseca
Norquist, Joseph L. .....St. Paul
Norris, John C. .....Mankato
Norval, Mildred A. .....Minneapolis
Nuebel, Charles J. .....Long Beach, CA
† Nuessle, Walter G. .....Springfield
Nuessle, William F. .....Minneapolis
Nydahl, Bruce C. .....Minneapolis
Nydahl, Malvin J. .....Minneapolis
† Nye, Lillian L. .....St. Paul
Nygren, William T. .....Braham
Nywall, Dean D. .....Slayton

O

O'Brien, Bruce J. .....Minneapolis
£ O'Brien, Charles P. .....Rochester
O'Brien, Gerald R. .....Minneapolis
O'Brien, John C. .....St. Paul
O'Brien, Louis T. .....Breckenridge
O'Brien, William A. .....Minneapolis
O'Byrne, Alvaro .....Mankato
† O'Donnell, James E. .....Minneapolis
O'Hanlon, William J. .....Minneapolis
O'Kane, Thomas W. .....St. Paul
O'Keefe, James P. .....St. Cloud
O'Leary, John B. .....Minneapolis
O'Malley, Valentine .....St. Paul
O'Neil, Bernerd L. .....Minneapolis
O'Neill, John C. .....Duluth
O'Neill, Nial C. .....St. Paul
O'Phelan, E. Harvey .....Minneapolis
† O'Reilley, Bernard E. .....Sun City, AZ
O'Rourke, William J. .....Austin
Obetz, Samuel W. .....Rochester
Ockuly, Orville E. .....St. Paul
Odland, Donald M. .....Luverne
Odland, Mark E. .....Detroit Lakes
Odland, Olin M. .....Marshall
£ Odyniec, Norman A. .....Rochester
Oeljen, Siegfried C. .....Waseca
Officer, Charles D. .....Burnsville
† Ogden, Warner .....River Falls, WI
† Ohage, Justus .....St. Paul
Ohmann, Ronald J. .....Minneapolis
Olavs, Olga .....Minneapolis
Olds, George H. .....New Richland
Olfelt, Paul C. .....Minneapolis
Olinger, John N. .....St. Cloud
† Olmanson, Edmund G. .....St. Peter
Olmanson, M. Donald .....St. Peter
Olmanson, Vern C. .....St. Peter
Olsen, Arthur M. .....Rochester
† Olsen, E. George .....Minnetonka
Olsen, Jay R. .....Minneapolis
Olsen, Ralph L. .....St. Paul
Olson, Albert J. .....Owatonna
Olson, Alton C. .....Minneapolis
Olson, Barbara F. .....Minneapolis
Olson, C. Kent .....Minneapolis
Olson, Carl J. .....Minneapolis
Olson, Detlof M. .....Minneapolis
Olson, Duane C. .....Minneapolis
Olson, Frances P. .....Fergus Falls
Olson, Grant E. .....West Concord
Olson, Hardin E. .....Minneapolis
£ Olson, John D. .....Rochester
Olson, Lillian A. .....Ah-Gwah-Ching
Olson, Neal R. .....Rochester
† Olson, Olof A. .....Minneapolis
Olson, Philip A. .....Minneapolis
Olson, Richard E. .....Chaska
Olson, Richard T. .....Virginia
Olson, Robert A. .....Minneapolis
Olson, Robert E. .....Minneapolis
Olson, Robert W. .....Minneapolis
Olson, Rolland A. .....Wayzata
Onofrio, Burton M. .....Rochester
† Onsgard, L. Kenneth .....St. Petersburg, FL
Opel, D. Douglas .....Rochester
£ Opgrande, John D. .....Rochester
Opheim, Richard H. .....Minneapolis
Opitz, Joachim L. .....Rochester
† Oppegaard, C. L. .....Scottsdale, AZ
Oppen, E. Gerhard .....Minneapolis
Oppen, Melvin G. .....Minnetonka
Opsahl, Lawrence J. .....Willmar
Opstad, Earl T. .....Minneapolis
Orandi, Ahmad .....Fergus Falls
Orandi, Mehdi .....Fergus Falls
Orbuch, Martin W. .....Minneapolis
Orkin, Milton .....Minneapolis
Orn, Duane L. .....Minneapolis
Orr, Burton A. .....Faribault
Osekowsky, Henry J. .....St. Paul
Osmundson, Philip J. .....Rochester
Osterberg, Kenneth A. .....Minneapolis
† Ostergaard, Erling .....Elbow Lake
Ostrov, Charles S. .....Minneapolis
Ott, Eugene C. .....Minneapolis
Ouellette, Alfred J. .....St. Paul
Ourada, Anthony L. .....Buffalo
Overgaard, Peter H., Jr. .....Lindstrom
Owen, Charles A., Jr. .....Rochester
Owen, Richard R. .....Minneapolis
Owens, Ben P. .....Hibbing
Owens, Frederick M. .....St. Paul
Owens, William A. .....Montevideo
£ Oxman, Herbert A. .....Rochester

P

Paal, Dwain J. ..... Minneapolis
Paciotti, Vincent J. ..... Hibbing
† Page, Raymond L. ..... St. Paul
£ Pairolero, Peter C. ..... Rochester
Paisner, Hyman M. ..... Minneapolis
Palattao, Agustin D., Jr. ..... Waconia
Palen, Benjamin J. ..... Scottsdale, AZ
Palm, E. Theodore ..... Minneapolis
Palm, Neil M. ..... St. Paul
† Palmer, Clinton F. ..... Albert Lea
Palmer, Harry A. ..... Blackduck
Palumbo, Pasquale J. ..... Rochester
Panning, Wayne P. ..... Marshall
Paparella, Michael M. ..... Minneapolis
Papermaster, Ralph ..... Minneapolis
Papermaster, Theodore C. ..... Wayzata
† Paradis, Gaston R. ..... Rochester
Park, Wilford E. ..... Minneapolis
Parker, Robert L. ..... Rochester
Parker, Warren E. ..... Sebeka
Parker, Wilbert H. ..... Chisholm
† Parkhill, Edith M. ..... Rochester
Parod, John D. ..... Minneapolis
Parra, Samuel ..... Crookston
Parrott, John C. ..... Minneapolis
£ Parry, Rodney R. ..... Rochester
Parson, E. Irvine ..... Duluth
Parsons, R. A. ..... St. James
Parsons, Ralph L. ..... Trimont
Pasek, Antone W. ..... Cloquet
Passmore, James A. ..... Ft. Sam Houston, TX
Patch, Orien B. ..... Duluth
£ Patrick, Donald L. ..... Rochester
Pattee, James J. ..... Minneapolis
Patten, John C. ..... Austin
Patterson, Hugh D. ..... Slayton
¶ Patterson, Linda G. ..... Rochester
Patterson, Paul G. ..... Minneapolis
Paule, William J. ..... Minneapolis
Paulson, Elmer C. ..... St. Paul
Paulson, Wallace J. ..... St. Paul
Payne, Richard E. ..... Virginia
Payne, W. Spencer ..... Rochester
Peake, Janna Z. ..... St. Paul
Pearson, Bror F. ..... Shakopee
† Pearson, Fritz R. ..... St. Paul
Pearson, Harris L. ..... Bagley
Pearson, Malcolm M. ..... St. Paul
† Pease, Gertrude L. ..... Rochester
† Pedersen, Arthur H. ..... St. Paul
Pedersen, Robert L. ..... Brainerd
Peikert, Carl F. ..... Forest Lake
Pelletier, Rene W. ..... St. Paul
Peluso, Charles R. ..... Minneapolis
Pelzl, Charles R. ..... Pine River
Penk, Engward L. ..... Springfield
Penn, George E. ..... Mankato
Pennington, Mary ..... Minneapolis
Peper, Martin C. ..... Minneapolis
Perkins, Douglass E. ..... Alexandria
Perlman, Everett C. ..... Minneapolis
Perlman, Herschel L. ..... St. Louis Park
Perry, Harold O. ..... Rochester
Perry, John F., Jr. ..... St. Paul
Perry, Lawrence B. ..... Rochester
Person, Duane F. ..... Virginia
Pesonen, Clifford ..... Austin
Peteler, Jennings, C. L. ..... Minneapolis
Peters, Gustavus A. ..... Rochester
Petersen, Byron D. ..... Minneapolis
Petersen, Deane A. ..... Wayzata
Petersen, Donald H. ..... Willmar
£ Petersen, Eugene G. ..... Rochester
Petersen, Glenn L. ..... Minneapolis
£ Petersen, Kenneth ..... Portland, OR
† Petersen, Magnus C. ..... Rochester
Petersen, Robert T. ..... St. Cloud
Petersen, William E. ..... Minneapolis
Peterson, Alvin C. ..... Mora
Peterson, Charles A. ..... Minneapolis
Peterson, Charles R. ..... Minneapolis
Peterson, Donald H. ..... St. Paul
Peterson, Edward A. ..... St. Paul
† Peterson, Edward N. ..... Virginia
Peterson, Hamlet A. ..... Rochester
Peterson, Harold O. ..... Minneapolis
*† Peterson, Joel L. E. ..... St. Paul
Peterson, John A. ..... Minneapolis
Peterson, John H. ..... Duluth
Peterson, John O. H. ..... Hastings
Peterson, John R. ..... Rushford
Peterson, Kenneth A. ..... Marshall
Peterson, Kenneth H. ..... Hutchinson
Peterson, Lowell F. A. ..... Rochester
Peterson, Oliver H., Jr. ..... Minneapolis
Peterson, Palmer A. ..... Minneapolis
Peterson, Rodney H. ..... Minneapolis
† Peterson, Roy A. ..... Vesta
Peterson, Roy L. ..... White Bear Lake
Peterson, Theodore A. ..... Minneapolis
Peterson, Willard C., Jr. ..... Minneapolis
Peterson, Willard E. ..... Willmar
Petit, Julien V. ..... Minneapolis
† Petit, Leon J. ..... Minneapolis
Petitt, Robert M. ..... Rochester
† Petraborg, Harvey T. ..... Aitkin
Pettersen, George R. ..... USS Hope
Pettko, Joseph ..... Wheaton
£ Petty, Roy W. ..... Rochester
Pewters, John T. ..... Minneapolis
Peyla, Thomas L. ..... Rochester
£ Pfaffenbach, David D. ..... Rochester
Pfohl, Richard A. ..... Minneapolis
Phares, Otto C. ..... St. Cloud
† Phelps, Kenneth A. ..... Palo Alto, CA
Phelps, Robert D. ..... Minneapolis
Phibbs, Clifford M., Jr. ..... Minneapolis
Phillips, Leonard ..... St. Paul
Philp, David R. ..... Watertown
£ Pien, Francis, D. ..... Rochester
Pierce, Robert B. ..... Heron Lake
Pierre, Robert V. ..... Rochester
Pierson, Roy F. ..... Slayton
Pietan, Jerold H. ..... Chisholm
£ Pikler, George M. ..... Rochester
Pilling, Loran F. ..... Minneapolis
Pilney, Frank T. ..... St. Paul
Pincus, Mitchell ..... Minneapolis
Pinell, Octavio C. ..... Minneapolis
Pinsonneault, W. A. ..... Roseau

Pistulka, Rolland D ..... Chaska
Pitcher, Arlo L. ..... St. James
Pivac, Dragojla (Popovich) ..... Milwaukee, WI
Pizarro, Remi L. ..... Minneapolis
Plasha, Matthew K. ..... Coon Rapids
Plass, Herbert F. R. ..... Minneapolis
Pleissner, Karl W. ..... Minneapolis
£ Pliam, Michael B. ..... Rochester
Plimpton, Nathan C. ..... Minneapolis
Plotke, Harry L. ..... St. Paul
Plucker, Milton W. ..... Worthington
Pluth, James R. ..... Rochester
Pohl, John F. ..... Minneapolis
£ Poland, Jerome D. ..... Minneapolis
Polesky, Herbert F. ..... Minneapolis
Poley, Brooks J. ..... Minneapolis
Pollak, Kurt ..... Minneapolis
Pollard, William S. ..... Duluth
Polley, Howard F. ..... Rochester
Pollman, Stanley E. ..... Naha, Okinawa
Pollock, Anthony J. ..... Minneapolis
Polski, Paul G. ..... South St. Paul
† Polzak, James A. ..... Roseville
Pone, John J. ..... Minneapolis
Ponterio, James E. ..... Shakopee
† Pool, T. Lloyd ..... Rochester
Poole, James R. ..... North St. Paul
Popadiuk, Peter ..... Minneapolis
Pope, David A. ..... Janesville
Popoff, Russel G. ..... Graceville
Popowich, John G. ..... Minneapolis
† Poppe, Frederick H. ..... Miami, FL
Poppie, Robert W. ..... Brainerd
£ Port, Friedrich K. ..... Rochester
Post, Edmund A. ..... St. Paul
Poston, Lawrence M. ..... Caledonia
Potter, Robert B. ..... Minneapolis
Pougiales, Mary L. ..... Rochester
£ Powell, David F. ..... Rochester
Power, John E. ..... Duluth
Powers, Robert L. ..... St. Paul
Pozuelo, Utanda, Jose ..... Rochester
† Pratt, Fred J. ..... Minneapolis
Pratt, Joseph H., Jr. ..... Rochester
Prentice, James A. ..... Rochester
£ Prentice, Linda G. ..... Rochester
Prentice, Walter B. ..... St. Paul
Prem, Konald A. ..... Minneapolis
Preston, Frank S., Jr. ..... Minneapolis
Price, William E. ..... Minneapolis
Prickman, William E. ..... Minneapolis
Priest, Robert E. ..... Minneapolis
† Priestley, James T. ..... Rochester
£ Pritchard, Douglas J. ..... Rochester
Prlina, Issac M. ..... Virginia
Proeschel, Ray K. ..... Willmar
Proshek, Lumir C. ..... Minneapolis
Proud, Harry S. ..... St. Paul
Provence, Cecil L. ..... Waconia
Pruitt, Raymond D. ..... Rochester
Pugh, David G. ..... Rochester
Pulido, Ernesto D. ..... Fergus Falls
Pumala, Erven E. ..... Warren
Purdie, James L. ..... Forest Lake
Purnell, Don C. ..... Rochester
Purves, G. Harland ..... Buffalo
Puumala, Barbara M. ..... Cloquet
Puumala, Reino H. ..... Cloquet
Puumala, Ricard R. ..... Cloquet

Q

Quattlebaum, Frank W. ..... St. Paul
Quello, Robert O. B. ..... Minneapolis
Quiggle, Arthur B. ..... Minneapolis
£ Quiroz, Salvador E. ..... Rochester
Quist, Henry W., Jr. ..... Minneapolis

R

Raab, David E. ..... Minneapolis
Raaen, Olaf J. ..... St. Paul
Rabcevich, Anatole ..... St. Paul
Racer, Harley J. ..... Minneapolis
Radke, Robert L. ..... Milan
£ Radtke, Wallace E. ..... Rochester
Raetz, Sylvester J. ..... Maple Lake
£ Rahimi, Abbas ..... Rochester
Raich, John J. ..... Minneapolis
Raile, Richard B. ..... Minneapolis
£ Raimundo, Hugo Sa ..... Rochester
Ralph, James R. ..... St. Paul
Ralston, Donald E. ..... Rochester
Ramlow, Ralph M. ..... West St. Paul
£ Ramos, Raul ..... Rochester
† Ramsey, Walter R. ..... St. Paul
Randall, David A. ..... Minneapolis
£ Randall, Patricia ..... Minneapolis
Randall, Raymond V. ..... Rochester
Ransom, H. Robert ..... Osseo
Ratelle, Alexander E. ..... Minneapolis
Raths, Otto N., Jr. ..... St. Paul
£ Rauenhorst, John M. ..... St. Paul
Ravits, Harold G. ..... St. Paul
Rayer, Anthony L. ..... Babbitt
Rayner, Ralph R. ..... Red Wing
Rea, Charles E. ..... St. Paul
Reardon, Andrew E. ..... Duluth
Recht, Thomas M. ..... Minneapolis
£ Reckles, Lawrence N. ..... Rochester
Redleaf, Paul D. ..... St. Paul
Reeber, Erick ..... Bagley
Reece, Richard L. ..... Minneapolis
Reed, Henry H. ..... Duluth

Reed, John H., Jr. ..... Minneapolis
Reed, Paul ..... Virginia
Reed, Sheldon C. ..... Minneapolis
Reese, David F. ..... Rochester
Reff, Alan R. ..... Crookston
Regan, John J. ..... Minneapolis
Rehmann, Ronald E. ..... Coon Rapids
Reichel, Samuel M. ..... Minneapolis
† Reichelderfer, Charles F. ..... Staples
Reichelt, Leland G. ..... Wadena
£ Reick, Robert R. ..... Rochester
Reid, Howard C. ..... Bemidji
Reid, James W. ..... South St. Paul
Reif, Harold A. ..... Minneapolis
Reif, Robert W. ..... White Bear Lake
Reiley, Richard E. ..... Minneapolis
Reilly, William F., Jr. ..... Davis-Monthan AFB, AZ
Reiners, Gary L. ..... Cambridge
Reinhardt, James H. ..... Alexandria
Reinhart, Richard O. ..... Minneapolis
Reisdorf, George E. ..... Minneapolis
Reiser, Milton P. ..... Minneapolis
Reitemeier, Richard J. ..... Rochester
ReMine, William H., Jr. ..... Rochester
Remole, William D. ..... Minneapolis
Resch, Joseph A. ..... Minneapolis
Restall, Charles J. ..... Rochester
Reynolds, Dermot F. ..... Hibbing
Reynolds, James C. ..... San Antonio, TX
Reynolds, James F. ..... Minneapolis
Rholl, Arnold O. ..... Minneapolis
Rhoton, Albert L. ..... Rochester
Rice, Carl O. ..... Minneapolis
Rice, Edwin G. ..... Minneapolis
Rice, Fred A. ..... Minneapolis
Rice, Hagbart G. ..... Moorhead
Rice, William H. ..... St. Cloud
† Richards, William B. ..... St. Cloud
Richardson, Edward J. ..... St. Paul
Richardson, Robert J. ..... Minneapolis
† Richdorf, Lawrence F. ..... Minneapolis
Richter, David J. ..... Virginia
Richter, Paul H. ..... Fergus Falls
Rick, Paul F. W. ..... St. Paul
Rierson, Phillip A. ..... Minneapolis
Rieschl, Elizabeth K. ..... Jordan
Rifat, Baseem M. ..... Clarkfield
Riggs, B. Lawrence ..... Rochester
Riley, Fenwick C., Jr. ..... Rochester
Riley, John D. ..... Minneapolis
Rimas, Matthew J. ..... Comfrey
Ringhofer, Lawrence ..... New Ulm
† Ringle, Otto F. ..... Walker
Rinkey, Eugene ..... St. Paul
Riordan, Elsie M. ..... Minneapolis
† Ripple, Rudolph J. ..... St. Paul
Ripple, Rudolph J., Jr. ..... Minneapolis
Risch, Ronald E. ..... Minneapolis
Risser, Alden F. ..... Stewartville
Ristic, Miodrag ..... Cambridge
Ritchie, Donald A. ..... St. Cloud
† Ritt, Albert E. ..... St. Paul
Ritter, Donald G. ..... Rochester
Rivan, Robert J. ..... Rochester
£ Rivers, Thomas A. ..... Rochester
Rizer, Dean K. ..... Minneapolis
Roach, Charles A. ..... St. Paul
Roach, Donald E. ..... St. Paul
† Robb, Edwin F. ..... Minneapolis
* Robbins, Owen F. ..... Minneapolis
Roberts, Byron H. ..... Minneapolis
Roberts, George A. ..... Austin
Roberts, Lewis J. ..... Minneapolis
† Roberts, Oliver W. ..... Owatonna
Robertson, Dennis M. ..... Rochester
† Robertson, Paul A. ..... Austin
£ Robertson, Robert C. ..... Rochester
Robinson, Cortland O. ..... Minneapolis
Robinson, William W. ..... Agana, Guam
Robnik, Spencer L. ..... Willmar
Rock, William H. ..... Anoka
Rocknem, Robert E. ..... Minneapolis
Rockwell, Curtiss V. ..... Minneapolis
Rockwood, Philo H. ..... Fergus Falls
£ Rodarte, Joe R. ..... Rochester
Rodgers, Richard S. ..... Minneapolis
† Roehlke, Arthur B. ..... Elk River
Roemer, Henry J. ..... Winona
Rogers, Charles W. ..... Winona
£ Rogers, Roy S., III ..... Rochester
Rogin, Norton ..... Minneapolis
† Roholt, Christian ..... McIntosh
Roholt, Hartvig B. ..... Bemidji
† Rohrer, Christian A. ..... Madison Lake
Rolig, David H. ..... West St. Paul
Rollins, Pat ..... Minnetonka
Rome, Howard P. ..... Rochester
Romero, Jose B. ..... St. Paul
Romness, Kenneth B. ..... Mound
Rooke, E. Douglas ..... Rochester
Rorem, Joseph A. ..... Appleton
Rose, Cordt ..... Albert Lea
£ Rosenbaum, Alan H. ..... Rochester
Rosenbaum, David L. ..... Minneapolis
£ Rosenbaum, Robert A. ..... Rochester
Rosendahl, Frederick G. ..... Minneapolis
† Rosenfield, Abraham B. ..... Minneapolis
Rosenquist, Rudolph J. ..... Minneapolis
Rosenow, Edward C., III ..... Rochester
Rosenow, John H. ..... Minneapolis
Rosenstein, Hanan J. ..... Minneapolis
† Rosenthal, Robert ..... St. Paul
† Rosenwald, Reuben M. ..... Anoka
Rosevear, John W. ..... Minneapolis
Ross, James V., Jr. ..... Rochester
Rossberg, Raymond A. ..... Morris
Rossen, Ralph X. ..... Minneapolis
Rotenberg, Robert J. ..... Minneapolis
Rotenberg, Samuel ..... Beverly Hills, CA
Roth, Albert H. ..... Deer River
Roth, Charles W. ..... Red Wing
Roth, Frederick D. ..... Mankato
Roth, George C. ..... St. Paul
£ Roth, George R., Jr. ..... Rochester
Rothnem, Morris S. ..... Minneapolis
Roust, Henry A. ..... Montevideo
Rovelstad, Randolph A. ..... Rochester
Rovelstad, Roger A. ..... St. Cloud
Rowe, Clarence J., Jr. ..... St. Paul
Rowe, Richard G. ..... Duluth
† Rowles, Everett C. ..... Laguna Hills, CA
Roy, Paul H. J. ..... Quebec, Canada
Roy, Philemon C. ..... St. Paul
Rozeboom, Paul E. ..... Mankato
Rozycki, Anthony T. ..... St. Cloud
Rubin, Manly ..... Minneapolis
Ruchie, Warren H. ..... Willmar
† Rucker, Charles W. ..... Rochester

Rucker, Thomas K. ..... Minneapolis
† Rucker, William H. ..... Minneapolis
† Rud, Norman E. ..... Edina
Rud, Paul D. ..... Luverne
Rudie, Peter S. ..... Duluth
Rudie, William D. ..... Duluth
£ Rue, David S. ..... Rochester
Ruggles, George M. ..... Forest Lake
† Ruhberg, George N. ..... Santa Barbara, CA
Ruhe, Albert H. ..... Willmar
Ruiz, Ernest ..... Minneapolis
Rukavina, John G. ..... St. Paul
† Rumpf, Carl W. ..... Faribault
Runquist, John M. ..... Duluth
Runquist, Richard K. ..... Cambridge
Rushay, Arthur J. ..... White Bear Lake
Rushton, Joseph G. ..... Rochester
† Russ, Homer H. ..... Blue Earth
£ Russ, Homer H., Jr. ..... Rochester
£ Russell, Robert C. ..... Rochester
Russeth, Arthur N. ..... Minneapolis
Rusten, Elmer M. ..... Minneapolis
Rusterholz, Alan P. ..... St. Paul
Ruth, Bradley R. ..... Duluth
Rutledge, John B. ..... Detroit Lakes
† Rutledge, Lloyd H. ..... Detroit Lakes
Ryan, Edward A. ..... Duluth
† Ryan, John J. ..... St. Paul
Ryan, Joseph M. ..... St. Paul
Rydberg, John S. ..... Minneapolis
Ryding, Vincent ..... Ames, IA
Rydland, Arne D. ..... Minneapolis
Rygh, Harold N. ..... Atwater
† Rynearson, Edward H. ..... Rochester
Rynda, Edwin R. ..... New Prague
Rysgaard, George N. ..... Northfield

S

Sadd, Milton ..... Willmar
Saffert, Cornelius A. ..... New Ulm
St. Cyr, Harry M. ..... Minneapolis
St. Cyr, Kenneth J. ..... Minneapolis
£ Salanga, Virgilo D. ..... Rochester
Salassa, Robert M. ..... Rochester
Salchert, John J. ..... Minneapolis
Salk, Richard J. ..... Albany
Saliterman, Bernard I. ..... Minneapolis
Saloum, Lucille M. ..... Duluth
Salovich, Edward L. ..... Minneapolis
Salovich, Elmer R. ..... Minneapolis
† Salter, Reginald A. ..... Virginia
Salter, Wilson M. ..... Willmar
£ Samara, David J. ..... Rochester
Sams, W. Mitchell, Jr. ..... Rochester
Sanchez, Jose S. ..... Edina
Sand, Richard E. ..... St. Paul
Sandeen, Richard M. ..... Buffalo
*† Sandell, Samuel T. ..... Duluth
Sander, Frank V., Jr. ..... Rochester
Sander, John L. ..... Red Wing
Sanderson, David J. ..... Fergus Falls
Sanderson, David R. ..... Rochester
Sandkamp, Virgil A. ..... South St. Paul
Sandok, Burton A. ..... Rochester
Sandt, Karl E. ..... La Jolla, CA
† Sanfelippo, Peter M. ..... Rochester
Sanfilippo, Sylvester J. ..... Minneapolis
Sanford, John B. ..... Duluth
Sanford, Raymond A. ..... Mankato
Sargent, John H. ..... St. Paul
Sartor, Richard ..... Minneapolis
£ Satava, Richard M. ..... Rochester
Sather, Edgar L. ..... Fosston
Sather, George A. ..... Fosston
Sather, Richard N. ..... Fosston
Sather, Russell O. ..... Crookston
Sauer, Jean C. ..... Fort Snelling
Sauer, Robert L. ..... Preston
Sauer, William G. ..... Rochester
Savett, Laurence A. ..... St. Paul
£ Savoy, Leonard B. ..... Rochester
Sawtell, Robert R. ..... Rochester
Sawyer, Glen T. ..... Minneapolis
Sax, Milton H. ..... Duluth
Saxena, Krishna M. ..... St. Paul
Saxman, Gertrude E. O. ..... Ulen
Sayther, Keith D. ..... Minneapolis
Sborov, Abe M. ..... Minneapolis
€ Scallen, Edward S. ..... Rochester
Scallen, Raymond W. ..... Minneapolis
Scanlan, Patrick J. ..... Minneapolis
Scanlon, Hugh A. ..... Little Falls
Scanlon, Paul W. ..... Rochester
Schaar, Frances E. ..... Minneapolis
† Schade, Frederick L. ..... Santa Cruz, CA
† Schaefer, Joseph F. ..... Sun City, AZ
† Schaefer, Wesley G. ..... Minneapolis
Schafer, Charles F. ..... Winona
Schaffhausen, George E. ..... St. Paul
Schaffhausen, Irwin F. ..... Minneapolis
Schaffhausen, Mildred ..... Minneapolis
Schamber, Walter F. ..... St. Cloud
Scheidel, Alois M. ..... Mankato
Scherek, Jerome J. ..... St. Paul
Scherer, L. Raymond ..... Minneapolis
Scherling, Sidney S. ..... Minneapolis
Scheuneman, Allen F. ..... Thief River Falls
Schiele, Burtrum C. ..... Minneapolis
Schimelpfenig, George T. ..... Chaska
Schirber, Martin J. ..... Grand Rapids
Schirger, Alexander ..... Rochester
Schless, James M. ..... Minneapolis
Schissel, Gregory A. ..... Minneapolis
Schissel, Richard C. ..... Minneapolis
Schloff, Ivan ..... St. Paul
Schloff, Leonard D. ..... St. Paul
Schmid, John F. ..... Duluth
† Schmidt, Hilmar R. ..... Winona
Schmidt, Paul G. ..... Granite Falls
Schmidt, Ruben F. ..... Alden
Schmidt, W. Robert ..... Minneapolis
Schmidtke, Reinhardt L. ..... St. Paul
† Schmitt, S. C. ..... Fallbrook, CA
Schmitt, Tim B. ..... Browerville

Schmitz, Anthony A. ....Mankato
Schmitz, Everett J. ....St. Cloud
Schnabel, Norma B. ....Crookston
Schnabel, Robert F. ....Crookston
Schneck, Jack I. ....Minneapolis
Schnell, Frederick S. ....Litchfield
£ Schnur, Paul L. ....Rochester
Schochet, H. Laurence ....St. Paul
£ Schoenberg, Bruce S. ....Rochester
Schoenberger, P. B. ....Perham
Schoening, Herbert A. ....Minneapolis
Schoenwetter, William F. ....Minneapolis
Scholz, Donald A. ....Rochester
† Schons, Edward ....Minnetonka Beach
Schossow, George W. ....White Bear Lake
Schottler, Jerry L. ....Minneapolis
Schottler, Max E. ....Minneapolis
Schotzko, John R. ....Blue Earth
Schrantz, Robert D. ....Rochester
Schroeckenstein, Hugo F. ....St. Paul
Schroeder, Albert J. ....Minneapolis
Schroeder, Glenn E. ....Red Wing
£ Schroeder, James G. ....Rochester
£ Schroeder, Stephen B. ....Rochester
£ Schroeter, Arnold L. ....Rochester
Schulberg, Verne A. ....Minneapolis
Schultz, Alan K. ....Minneapolis
Schultz, Alvin L. ....Minneapolis
Schultz, J. Harold ....Minneapolis
Schultz, Paul E. ....St. Paul
Schultz, Peter J. ....Minneapolis
Schultz, Robert J. ....Minneapolis
Schulz, Jerome E. ....Stillwater
Schulz, Robert W. ....Fairmont
Schulze, William M. ....Minneapolis
Schumacher, John W. ....Minneapolis
£ Schumacher, Robert V. ....Minneapolis
*† Schut, John W. ....Anoka
Schut, Lawrence J. ....Minneapolis
Schutt, Allan J. ....Rochester
Schutt, Ann H. ....Rochester
† Schwab, Peter M. ....Rochester
¶ Schwartan, Neal W. ....Rochester
Schwartz, Carl A. ....Hastings
Schwartz, E. Robert ....Minneapolis
Schwartzkopff, Othild ....St. Paul
Schweiger, Theodore R. ....Hibbing
Schwinghamer, Thomas G. ....Ely
¶ Schwerman, Earl A., Jr. ....Rochester
Sciarra, John J. ....Minneapolis
Scott, Eugene E. ....St. Paul
Scott, Horace G. ....Minneapolis
¶ Scott, James J. ....Rochester
Scott, Robert H. ....Minneapolis
Scott William R. ....Minneapolis
† Seaberg, John A. ....Pequot Lakes
Seay, James E., III ....Minneapolis
Sebald, John R. ....Mankato
Seecamp, Carsten H. ....Cambridge
Seery, Thomas ....Rochester
£ Segal, Anthony ....Rochester
Segal, Edward L. ....Minneapolis
Segal, Martin A. ....Minneapolis
Segal, Marvin S. ....Minneapolis
Segal, Sheldon J. ....Minneapolis
£ Seghers, Victor K. ....Rochester
£ Segura, Joseph W. ....Rochester
† Seham, Max ....St. Paul
Seifert, Donald R. ....Little Falls
Seifert, Gregory L. ....Excelsio
*† Seifert, Milton H. ....Excelsio
Seifert, Milton H., Jr. ....Excelsio
Seisler, Edward P. ....Worthingto
£ Sejar, Joseph P. ....St. Pau
Sekhon, Mohan S. ....St. Pau
† Seldon, T. Harry ....Rocheste
Seljeskog, Edward L. ....Minneapoli
Sells, Richard J. ....St. Pau
Selmo, Joseph D. ....Norwoo
Semba, Thomas ....Minneapoli
Semsch, Robert D. ....Wayzat
£ Serafano, Donald N. ....Rocheste
Sessler, Alan D. ....Rocheste
Sethre, Arthur E. ....Fergus Fall
† Setzer, Hobert J. ....St. Pau
Setzer, Hobert J., Jr. ....Mankat
Severseike, Odean M. ....Minneapoli
Seymour, John L. ....Minneapoli
Shackelford, Terry C. ....Minneapoli
£ Shallal, John A. ....Rocheste
Shandorf, James F. ....Minneapoli
Shanks, James R. ....Minneapoli
† Shannon, William R. ....Faribaul
† Shaperman, Eva P. ....San Diego, C
Shapiro, Fred L. ....Minneapoli
Shapiro, Irving ....Minneapoli
Shapiro, Sidney K. ....Minneapoli
Shapiro, Stanley W. ....Minneapoli
Shattuck, Clark A. ....Minneapoli
Shaver, Ward ....Fergus Fall
Shaw, Howard A. ....Minneapoli
Shea, Andrew W. ....Minneapoli
£ Shea, John A. ....Rochester
Shear, Howard H. ....St. Paul
£ Shearin, Robert P. N. ....Rochester
£ Sheehan, William C. ....Rochester
Shelander, Marcus I. ....St. Paul
Shemesh, Alvin ....Minneapolis
£ Shen, Fu-hsung ....Rochester
Shepard, Richard ....Albert Lea
Sheppard, Charles G. ....St. Peter
Sheps, Sheldon G. ....Rochester
Sher, David A. ....Virginia
Sher, Lewis ....Minneapolis
Sherman, Alfred G. ....Albert Lea
† Sherman, Carnot H. ....Bayport
Sherman, Lloyd F. ....Minneapolis
Sherman, Royal V. ....Red Wing
Shertzer, John H. ....Fort Bragg, NC
Shick, Richard M. ....Rochester
† Shillington, Maurice A. ....Ft. Lauderdale, FL
Shin, Rok ....Howard Lake
Shirley, Raymond M. ....Duluth
Sholler, Lawrence J. ....Minneapolis
Shragg, Robert I. ....Minneapolis
Shronts, John F. ....Minneapolis
Sidell, Franklin D. ....Minneapolis
£ Sidell, Peter M. ....Rochester
Siebert, Darrell W. ....Luverne
Siegel, Clarence ....St. Paul
Siegel, John S. ....Virginia
Siegel, Leighton G. ....St. Paul
Siegmann, William C. ....Minneapolis
Siekert, Robert G. ....Rochester
Sigel, Melvin E. ....Minneapolis
Silas, Ralph M. ....Minneapolis
Silver, John D. ....Minneapolis
Silverstein, Murray N. ....Rochester

Silverstein, Paul M. ....Minneapolis
Simison, Carl ....Barnesville
Simmonds, Harry N. L. ....St. Paul
£ Simmons, Paul B. ....Rochester
Simmons, Richard K. ....Minneapolis
Simmons, Richard L. ....Minneapolis
Simo, Kathleen Kay ....Minneapolis
Simons, John N. ....Rochester
Simons, Leander T. ....St. Paul
Simonson, Donald B. ....Minneapolis
Simso, Lee A. ....Minneapolis
Singer, Benjamin J. ....St. Paul
Singher, Lawrence J. ....Minneapolis
£ Singleton, Alice F. ....Rochester
Sinykin, Melvin B. ....Minneapolis
Sipe, James W. ....Coon Rapids
£ Sippe, Joseph L. ....Rochester
£ Siqueira, Aristarco ....Rochester
£ Sisco, Wm. T. ....Rochester
£ Sisemore, Daniel C. ....Rochester
Sisk, Harvey E. ....St. Cloud
† Sisler, Clifford E. ....Grand Rapids
£ Sizemore, Glen W. ....Rochester
Sjoding, J. Donald ....Mankato
Sjostrom, Lawrence E. ....St. Peter
† Skaggs, Harold, Jr. ....Rochester
Skinner, Abbott ....St. Paul
† Skinner, Harvey O. ....St. Paul
Skinner, Ira C., III ....San Antonio, TX
Skjold, Arthur C. ....Minneapolis
Skogerboe, Rudy ....Grand Forks, MN
Slack, William J. ....Duluth
Slanga, Roger A. ....St. Cloud
Sletten, Richard G. ....Minneapolis
£ Slocum, James R., Jr. ....Rochester
Slosser, Gaius J. ....Minneapolis
£ Smigiel, Mitchell R., Jr. ....Rochester
Smiley, Donald P. ....St. Paul
Smiley, John T. ....Minneapolis
Smisek, Elmer A. ....St. Paul
£ Smisek, Frank M. ....Minneapolis
£ Smith, Adam M. ....Minneapolis
Smith, Archie M. ....Minneapolis
Smith, Barlow ....Minneapolis
Smith, Baxter A., Jr. ....Minneapolis
Smith, Cyril M. ....Duluth
Smith, Don V. ....Blue Earth
Smith, George R. ....Hutchinson
Smith, Graham G. ....Minneapolis
Smith, H. Nippert ....St. Paul
Smith, Harry J. ....Lake Crystal
Smith, Henry T. ....Minneapolis
£ Smith, J. Baldwin, III ....Rochester
£ Smith, James C. ....St. Paul
Smith, John E. ....Minneapolis
Smith, J. Weston ....St. Cloud
Smith, Lloyd A. ....Willmar
Smith, Lucian A. ....Rochester
Smith, Nadine G. ....Minneapolis
Smith, Ralph E. ....Rochester
£ Smith, Ronald E. ....Rochester
Smith, Theodore S. ....Minneapolis
Smith, Thorsten ....Thiells, NY
£ Smith, V. Roy ....Rochester
Smith, Vernon D. E. ....St. Paul
Smith, Wallace R. ....Grand Marais
Smith, William T. ....St. Paul
Smorstok, Matthew B. ....Monticello
Smyth, John J. ....Lester Prairie
† Smythe, Gwendolyn S. ....Austin
Snider, Howard R. ....Mankato
† Snyder, George W. ....St. Paul
Snyder, Robert E. ....Spring Valley
† Snyker, Omer E. ....Ely
Soderberg, Richard J. ....Minneapolis
† Soderlind, Ragnar T. ....Minneapolis
£ Soderstrom, Carl W., Jr. ....Rochester
† Sohlberg, Olof I. ....St. Paul
Soiseth, Robert P. ....Minneapolis
Solhaug, Samuel B., Jr. ....Minneapolis
Soll, Robert W. ....Minneapolis
£ Solley, Graham O. ....Rochester
Solvason, Harold M. ....Minneapolis
£ Somerville, Gordon W. ....Rochester
Sommer, R. K. ....Elk River
Sommerdorf, Vernon L. ....St. Paul
Sommers, Stephen D. ....St. Cloud
£ Sondag, Glenn E. ....Rochester
Sondreal, Wesley D. ....Bemidji
Sones, Donald A. ....Rochester
£ Sonnemaker, Robert E. ....Rochester
Sonnesyn, Nels N. ....Le Sueur
Sontag, David W. ....Lake City
Sorem, Milton B. ....St. Paul
Soriano, Dominador B. ....Onamia
£ Soriya, Lashman W. ....Rochester
Soucheray, Philip H. ....St. Paul
Sosey, Walter K. ....Crosby
Soule, Edward H. ....Rochester
† Souster, Benjamin B. ....St. Paul
Sowada, Ernest J. ....St. Paul
Spagnolo, Anthony A. ....Shakopee
† Spang, Anthony J. ....Duluth
† Spang, James S. ....Duluth
Spang, William M. ....Duluth
Spano, Joseph P. ....Minneapolis
Speckhals, Robert C. ....Faribault
£ Speirs, Harvey R. ....Rochester
Spencer, Bernard J. ....Minneapolis
Spencer, David L. ....Anoka
Spencer, Joseph F. ....Duluth
Spencer, Robert J. ....Rochester
Spenny, Edward A. L. ....Minneapolis
Sperl, Michael P., Jr. ....St. Paul
Spiekerman, Ralph E. ....Rochester
Spieler, F. B. ....Pequot Lakes
£ Spil, Samuel ....Rochester
Spink, Wesley W. ....Minneapolis
Spittell, John A., Jr. ....Rochester
Sponsel, Kenath H. ....Minneapolis
Sprafka, Gregory A. ....St. Paul
Sprafka, Joseph L. ....St. Paul
† Sprague, Randall G. ....Rochester
Spraitz, Anton F., Jr. ....St. Paul
† Spurzem, Raymond J. ....Anoka
£ Srikumpol, Ananta ....Rochester
Stadem, Clifford J. ....Crookston
Stafne, John G. ....St. Paul
Stahl, George W. ....Austin
Stahler, Paul A. ....Jordan
Stahn, Louis H. ....St. Cloud
Stahr, Aubrey C. ....Hopkins
Stam, John ....Worthington
Standefer, James E. ....Minneapolis
† Stanford, Charles E. ....Elcho, WI
£ Staryk, Steven E., Jr. ....Rochester
† Stauffer, Maurice H. ....Rochester
Stecker, Raymond H. ....APO New York, NY
£ Steffee, William P. ....Rochester

£ Stehr, Christian H. ..... Rochester
Steidl, Richard M. ..... Minneapolis
£ Stein, Paul S. ..... Rochester
† Stein, Raymond J. ..... Pierz
Stein, Robert L. ..... Tyler
Stein, William A. ..... Duluth
Steinberg, Charles L. ..... St. Paul
Steiner, Andrew M. ..... St. Michael
Steiner, Leon E. ..... Albert Lea
£ Steiner, Terrance R. ..... Rochester
£ Steinfeld, Carroll M. ..... Rochester
Steinhilber, Richard M. ..... Rochester
† Stelter, Lloyd A. ..... Minneapolis
Stemsrud, Harold L. ..... Alexandria
† Stenstrom, Annette T. ..... Grand Marais
Stenzel, Donald A. ..... Minneapolis
Stenzel, Joseph A. ..... Minneapolis
Stephens, William E. ..... Minneapolis
Stern, Barry L. ..... San Antonio, TX
Sterner, Donald C. ..... St. Paul
* Sterner, Ernest R. ..... St. Paul
Sterner, John J. ..... St. Paul
Sterrie, Norman A. ..... Minneapolis
£ Stevens, John W. ..... Rochester
Stevens, Sheridan S. H. ..... Minneapolis
Stewart, Donald E. ..... Crookston
£ Stewart, John W. ..... Rochester
Stewart, Marvin J. ..... Minneapolis
Stewart, Paul B. ..... Minneapolis
Stickney, J. M. ..... Rochester
Stiegler, Farrell S. ..... Minneapolis
Stifter, Anton J. ..... Winsted
Stiles, Clifford D. ..... Foley
Stillman, M. Thomas ..... Minneapolis
Stillwell, George K. ..... Rochester
† Stillwell, Walter C. ..... Mankato
† Stilwell, George G. ..... Rochester
£ Stine, Harold E. ..... Rochester
£ Stocker, Michael A. ..... Rochester
Stoker, Lynn C. ..... Albert Lea
Stolee, Thomas A. ..... St. Paul
Stolen, Keith H. ..... Grand Rapids
Stoltz, Robert C. ..... Minneapolis
Stone, Norman F. ..... Minneapolis
Stone, Stanley P. ..... Minneapolis
£ Stone, Stephen P. ..... Rochester
£ Stonnington, Henry H. ..... Rochester
Storsteen, Kenneth A. ..... Duluth
Stover, Laddie E. ..... Marshall
Stoy, Robert A. ..... Little Falls
Strait, Herbert S. ..... Minneapolis
Strand, Clarence M. ..... Minneapolis
Strand, Jack W. ..... Jasper
Strand, Peter J. ..... Minneapolis
£ Strand, Richard C. ..... Bloomington
Strand, Roger W. ..... Willmar
Stransky, Theodore W. ..... Owatonna
Strathern, Carleton S. ..... St. Peter
† Stratte, Alf K. ..... Pine City
† Stratte, Harold C. ..... Windom
Stratte, Jon R. ..... Stillwater
Strauchler, John ..... Belview
Straus, Maurice L. ..... St. Paul
Street, Bernard ..... Northfield
Streitz, John M. ..... Duluth
Strem, Edward L. ..... St. Paul
Streu, Richard E. ..... Minneapolis
Strewler, Gordon J. ..... Duluth
Strickler, Jacob H. ..... Minneapolis
Strobel, Claire J. A. ..... Mankato
Strobel, Jack L. ..... Minneapolis
Stroebel, Charles F., Jr. ..... Rochester
Strom, Gordon W. ..... Minneapolis
Strom, Robert L. ..... Minneapolis
Stromgren, Delph T. ..... Minneapolis
Stromme, William B. ..... Minneapolis
Strong, Cameron G. ..... Rochester
Strough, LaVern C. ..... Worthington
Strouth, Jonas C. ..... Virginia
Strunk, Clarence A. ..... Minneapolis
Struthers, Lewis E. ..... Parkers Prairie
Stuber, Robert R. ..... St. Cloud
Student, Richard E. ..... Minneapolis
Studer, Donald J. ..... Faribault
Sturges, Robert L. ..... Minneapolis
Sturley, Rodney F. ..... St. Paul
£ Su, Philo S. ..... Rochester
Subak, Barbara H. ..... Minneapolis
Subby, Walter ..... Minneapolis
£ Suh, Ku Won ..... Rochester
Sukov, Marvin ..... Minneapolis
Sulciner, Aurel ..... Minnetonka
Sullivan, W. Albert, Jr. ..... St. Paul
Summar, M. Thomas ..... Virginia
Summerskill, William H. ..... Rochester
£ Sun, Nora C. J. ..... Rochester
Sundberg, A. Bruce ..... Minneapolis
Sundt, Thoralf M., Jr. ..... Rochester
£ Sung, David T. W. ..... Rochester
£ Suros, Juan ..... Rochester
Sutherland, John E. ..... Indian Head, MD
Svien, Hendrik J. ..... Rochester
Swaiman, Kenneth F. ..... Minneapolis
Swallen, Thomas O. ..... Minneapolis
† Swanson, David A. ..... Minneapolis
Swanson, David W. ..... Rochester
Swanson, Gerald E. ..... Minneapolis
£ Swanson, Gene E. ..... Rochester
Swanson, John O. ..... Minneapolis
Swanson, Lawrence J. ..... West St. Paul
Swanson, Ralph H. ..... West St. Paul
Swanson, Wallace L. ..... Richfield
Swedberg, William A. ..... Duluth
Swedenburg, Paul A. ..... Glenwood
† Sweetser, Horatio B. ..... Minneapolis
Sweetser, Theodore H., Jr. ..... Minneapolis
Swendseen, Carl J. ..... Minneapolis
† Swendson, James J. ..... St. Paul
Swensen, Don P. ..... Duluth
† Swenson, Arnold O. ..... Duluth
Swenson, Donald B. ..... St. Paul
Swenson, Donald B. ..... Mankato
Swenson, Floyd J. ..... Grand Rapids
Swenson, James D. ..... Edina
Swenson, Orville P. ..... Cloquet
Swenson, Richard W. ..... Minneapolis
Swenson, Roy G. ..... North Branch
Swift, Dean C. ..... Minneapolis
£ Swint, Robert E. ..... Rochester
£ Switz, Donald M. ..... Rochester
Symchych, Boris E. ..... Minneapolis
Syverson, Leslie A. ..... Fergus Falls

T

Taddeini, Luigi ..... St. Paul
Taintor, Ronald W. ..... Marshall
£ Tajik, Abdul J. ..... Rochester
£ Takahashi, Raymond ..... Rochester
Talsness, Jon M. ..... International Falls
Tam, Ernest C. ..... Minneapolis
Tambornino, Joseph M. ..... Minneapolis
Tan, Ruby ..... Marshall
Tanaka, Shin ..... Minneapolis
Tanasichuk, Murray A. ..... St. Paul
Tangedahl, Tim N. ..... Bismarck, ND
Tangen, George V. ..... Minneapolis
Tani, George T. ..... St. Paul
† Tanquist, Edwin J. ..... Alexandria
Tanquist, Edwin J., Jr. ..... Alexandria
£ Tapia, Hugo R. ..... Rochester
Taswell, Howard F. ..... Rochester
Tate, Wayne E. ..... South St. Paul
Taufic, Mansur ..... Austin
Tauxe, Welby N. ..... Rochester
† Taylor, Joseph H. ..... Ft. Lauderdale, FL
Taylor, Ross M. ..... Thief River Falls
Tchou, Mien-Fa ..... Minneapolis
Teeter, Richard R. ..... St. Paul
Teich, Kenneth W. ..... McKeesport, PA
Teisberg, John E. ..... St. Paul
Telander, Robert L. ..... Minneapolis
Tempel, J. W. ..... Blue Earth
ten Bensel, Robert W. ..... Minneapolis
Tenner, Robert J. ..... Minneapolis
Terrell, Bernard J. ..... Nopeming
Tesch, Gordon H. ..... Elk River
Teska, Byron A. ..... Minneapolis
Testor, James V. ..... Winona
Tetlie, James P. ..... Duluth
† Teunis, Bernard S. ..... Rochester
Teynor, Joseph W. ..... Minneapolis
Tharp, Ralph ..... Minneapolis
Thayer, Ellsworth A. ..... Fairmont
Thalhuber, Wayne H. ..... St. Paul
Thelemann, Arthur R., Jr. ..... Minneapolis
Theobalt, Inge M. ..... Minneapolis
Theologides, Anthanasios ..... Minneapolis
† Thielen, R. D. ..... New Brighton
Thiem, Chester E. ..... Mankato
Thienes, R. Lawrence ..... St. Cloud
Thomas, John V. ..... Duluth
Thomas, Juergen E. ..... Rochester
£ Thomas, William F., III ..... Rochester
Thomas, William H. ..... Minnetonka
Thomasson, Robert D. ..... Minneapolis
Thomes, A. Boyd ..... Minneapolis
Thompson, Arthur ..... Minneapolis
Thompson, A. Henry ..... St. Peter
¶ Thompson, Conrad O. ..... Rochester
Thompson, Carl O. ..... Hendricks
† Thompson, Gershom J. ..... Rochester
Thompson, James I. ..... Duluth
Thompson, James R. ..... Bemidji
Thompson, Paul E. ..... Long Prairie
£ Thompson, Robert R. ..... Rochester
Thompson, Russell A. ..... Willmar
Thompson, Thoburn F. ..... Albert Lea
Thompson, V. James ..... Staples
Thompson, Wayne W. ..... St. Paul
† Thompson, James M. ..... St. Paul
† Thomson, James M. ..... St. Paul
Thorbus, Ruben S. ..... Karlstad
Thorsgard, Ernest O. ..... Thief River Falls
£ Throckmorton, Tom D. ..... Rochester
Thurber, Deloran L. ..... Rochester
Thurn, Roy J. ..... Duluth
Thysell, Desmond M. ..... Minneapolis
Thysell, Vernon D. ..... Moorhead
£ Tiede, James J. ..... Rochester
Tierney, Jon P. ..... Minneapolis
Tietz, Charles A. ..... Virginia
Tiffany, Francis B. ..... St. Paul
Tifft, Cyril R. ..... St. Paul
† Tillisch, Jan H. ..... Rochester
Timm, Marvin E. ..... Wabasha
£ Tindel, Jerry R. ..... Rochester
Tinkham, Robert G. ..... Rochester
£ Tinstman, Thomas C. ..... Rochester
Titrud, Leonard A. ..... Minneapolis
Tobin, John A. ..... Minneapolis
Tobin, John D. ..... Minneapolis
Todd, John C. ..... Austin
Tompkins, Richard B. ..... Rochester
Tongen, Lyle A. ..... St. Paul
Torres, Fernando ..... Minneapolis
Torp, William B. ..... Minneapolis
Tosseland, Noel E. ..... Duluth
£ Totz, Robert S. ..... Rochester
† Town, Louise A. ..... Minneapolis
Townes, C. Dwight, Jr. ..... Minneapolis
Townsend, Gary L. ..... Rochester
Trach, Benedict B. ..... Minneapolis
† Traeger, Carl A. ..... Faribault
Trajano, Lorenz F. ..... Fergus Falls
Trautmann, James C. ..... Rochester
Travis, James S. ..... St. Paul
Travis, Richard C. ..... Elk River
Treanor, Thomas A. ..... Albert Lea
Treat, William A. ..... Minneapolis
Tregilgas, Richard B. ..... St. Paul
£ Tressler, Hubert A. ..... Rochester
*† Troost, H. Bradley ..... Mankato
Trost, Francis J. ..... Minneapolis
Trotman, Neil M. ..... St. Paul
Troup, Elliott V. ..... St. Paul
Trow, James E. ..... Minneapolis
Trow, William H. ..... St. Paul
£ Trowbridge, Arthur A., Jr. ..... Rochester
Trudeau, David ..... Austin
Truesdale, Clark W. ..... Glencoe
Tsai, Shih Hao ..... Minneapolis
Tsairis, Peter ..... Bethesda, MD
Tschetter, Loren K. ..... Rochester
Tuason, Vincente ..... St. Paul
Tucker, Richard C. ..... Minneapolis
Tudor, Richard B. ..... Minneapolis
£ Tully, Timothy E. ..... Bloomington
Tuma, Benjamin M. ..... Faribault
Turbak, Charles E. ..... Minneapolis
Turkbas, Nejat ..... St. Paul
Tveten, Omar A. ..... St. Paul
Tweedy, John A. ..... Winona
Tweedy, Robert ..... Winona
Twidwell, Joseph E. ..... Minneapolis
Twiggs, Leo F. ..... Austin
Tyce, Francis A. ..... Rochester
Tygart, Robert L. ..... Duluth

U

Ubel, Frank A. ..... St. Paul
Uhley, Charles G. ..... Crookston
† Uihlein, Alfred ..... Rochester
Ulrich, Emery E. ..... Duluth
Ulrich, Wesley D. ..... Bethesda, MD
Ulvestad, Harold S. ..... Minneapolis
Undem, Dale ..... Alexandria
Underdahl, L. O. ..... Rochester
Urbanyi, Eugene W. ..... St. Cloud
Utendorfer, Robert W. ..... Minneapolis
Utz, David C. ..... Rochester
Utz, Philip H. ..... LaCrosse, WI

V

Vaaler, Robert T. ..... Minneapolis
Vaccarella, R. James ..... St. Paul
* Vail, David J. ..... St. Paul
Valgemae, Romil ..... Minneapolis
£ Vanasek, Richard J. ..... Rochester
Van Bergen, Frederick H. ..... Minneapolis
Van Cleve, Horatio P., Jr. ..... Austin
Van DeRiet, Lowell W. ..... St. Paul
¶ Van Groll, Sister Kathleen ..... Rochester
Vanderpool, Thomas E. ..... Paynesville
Vandersluis, Charles W. ..... Minneota
Van Dervoort, Robert L., Jr. ..... Carswell AFB, TX
Van Druten, William A. ..... Duluth
Van Herik, Martin ..... Rochester
† Van Meier, Henry ..... Stillwater
Van Ness, Noel T. ..... Columbia, SC
Van Nostrand, David M. ..... St. Cloud
£ Van Ooyen, Marinus ..... Rochester
Van Oppen, Dirk J. A. ..... Minneapolis
Van Puffelen, Paul S. ..... Duluth
Van Ryzin, Donald J. ..... Duluth
Van Tassel, Robert A. ..... Minneapolis
Varco, Richard L. ..... St. Paul
£ Vargas-Cortes, Fernando ..... Rochester
Vaughn, C. Gordon ..... St. Paul
Vaughn, Louis D. ..... Rochester
Veinbergs, Arnold ..... St. Paul
† Veirs, Dean M. ..... Hastings
Vellek, Donald G. ..... Minneapolis
† Venables, Alexander E. ..... Maryville, WA
Vener, John M. ..... Arlington
Venters, Homer D., Jr. ..... St. Paul
Veranth, Leonard A. ..... St. Cloud
† Vezina, John C. ..... Mapleton
Vieiralves, Gilson M. ..... Winona
Vik, A. Elliott ..... Minneapolis
Vilaseca, Louis B. ..... Minneapolis
£ Villanueva, Javier P. ..... Rochester
Virnig, Hildegard J. ..... Caledonia
Virnig, Mark P. ..... Wells
Virnig, Richard P. ..... Wells
¶ Visscher, Maurice B. ..... Minneapolis
Vogel, Ann C. ..... New Ulm
Vogel, Howard A. L. ..... New Ulm
Von Drashek, Joseph C. ..... Mankato
Von Drashek, Stanley C. ..... Minneapolis
Von Weiss, David L. ..... Minneapolis
Vorlicky, Loren N. ..... Minneapolis
Votel, Thomas W. ..... St. Paul

W

† Waas, Charles W. ..... St. Paul
Wagner, Christian J. ..... Minneapolis
Wagner, Norman W. ..... Benson
Wagner, Robert M. ..... Minneapolis
Wagoner, Richard D. ..... Rochester
Wahman, Robert E. ..... Duluth
Wahner, Heinz W. ..... Rochester
¶ Wakim, Khalil G. ..... Rochester
Walden, A. Don ..... LeSueur
Walder, Harold J. ..... Duluth
† Waldron, Carl W. ..... Scottsdale, AZ
Waldron, John F. ..... Minneapolis
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Section 2 of Two Sections

The Development of Thoracic Surgery in the Upper Mid-West

THOMAS J. KINSELLA, M.D.

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Thomas J. Kinsella, M.D.
(1895-1969)

Thomas J. Kinsella, M.D.

Dr. Thomas J. Kinsella in his last years after retiring from the active practice of thoracic surgery, occupied himself with a compilation of local events that constitute "The History of Thoracic Surgery in the Upper Mid-West." This history, excerpted from his voluminous records, is now published as a Supplement to MINNESOTA MEDICINE.

He played a major role in the development of thoracic surgery in the Mid-West, and no one was more familiar with the progressive changes in surgical techniques, pulmonary physiology and advances in anesthesia. Some of us, who had the opportunity of working with him and observing his ability first-hand, were able to appreciate his tremendous perseverance and talent along with his complete devotion to specialized surgical endeavors.

Surgical therapy for pulmonary problems developed originally as an attempt to improve the dismal results of medical treatment of tuberculosis. Non-surgical treatment included prolonged periods of strict bedrest and the use of artificial or induced pneumothorax, pneumoperitoneum and with or without phrenic nerve operations. Sanatoria for patients with pulmonary tuberculosis became centers for various chest surgical procedures aimed at correcting complications of medical care and adding additional collapse measures such as extrapleural pneumothorax, oleothorax of various types and eventually thoracoplasty. Frequently multiple collapse measures were used in the same patient as one or another of the initial efforts failed in "arresting" the disease.

We recollect the earliest beginnings of thoracoplasty when the speed with which the procedure was completed supposedly determined success or failure for the patient. Dr. Arthur A. Law, who preceded Tom Kinsella as chief surgeon at Glen Lake Sanatorium, always used a stop watch to check his time and woe befell the assistants if more time elapsed than planned.

It remained for Tom to disprove the "speed" theory, which prevailed for many years. He demonstrated conclusively that patients had a smoother postoperative course when careful and meticulous anatomic dissection was performed regardless of the length of time required. This was true whether the operation was done under local or general anesthesia. Many old timers remember with amusement his personal dehydration training course in an attempt to delay certain vital functions whenever he planned a prolonged surgical procedure. At times a relief crew of nursing assistants became necessary because of exhaustion. Tom never seemed to tire.

When he left the Sanatorium to enter private practice, he transferred his clinical work to St. Mary's Hospital in Minneapolis although he continued to maintain the surgical program at the Glen Lake Sanatorium. Finally, resection of lung tissue became feasible due to increasing knowledge of pulmonary physiology leading to safer anesthesia, as well as increasing recognition of the importance of preoperative and postoperative care. Bronchoscopy, bronchograms and accessory surgical diagnostic measures led to further successful development of lung resection. These efforts were furthered by the discovery of chemotherapeutic agents which assisted in reducing and often eliminating surgical complications. These favorable events then permitted the extension of definitive thoracic surgical procedures to many other acute and chronic pulmonary conditions besides tuberculosis. While many of the improvements in surgical knowledge and techniques were used initially in lung surgery, they eventually led to remarkable progress in cardiac and other areas of major surgery.

Kinsella loved to teach. He was never too busy to explain the condition of a patient or his operative plans or his surgical technique to the youngest student nurse or the newest intern as well as to his medical colleagues.

Dr. Kinsella was a master surgical technician, but his surgical ability was enhanced by his experience in the medical care of patients with tuberculosis. His knowledge of total care led to a better understanding of all the difficulties in achieving satisfactory end-results and the value of team efforts in solving surgical problems.

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The Development of Thoracic Surgery in the Upper Mid-West

THOMAS J. KINSELLA, M.D.

"Then the Lord God cast a deep sleep upon Adam: and when he was fast asleep he took one of his ribs, and filled up flesh for it. And the Lord God built the rib which he took from Adam into a woman: and brought her to Adam." Genesis 2:21-22.

THUS, DIVINELY conceived and executed was the first surgical operation and Thoracic Surgery established by the Supreme Anesthesiologist-Surgeon.[204] Now thousands of years later the practitioners of this surgical specialty have accomplished wonders, almost miracles. They even are accused of usurping the prerogatives of the Almighty. Be that as it may, the results obtained fall far short of the original operation.

Throughout the ages knowledge and experience accumulated slowly and intermittently with much loss in the intervening time. Drainage of purulent accumulations apparently came first. The Hippocratic[216] school in the fourth century B.C. recognized empyema and pyopneumothorax with its "Hippocratic succussion splash" and established drainage, even advising injection of air into the pleural cavity to facilitate removal of the pus.

Paul[306] of Aegina (625-690 A.D.) advised paracentesis but did not open the chest. Lanfranchi[228] of Milan in his Chirurgia Magna 1296 mentions operations for empyema. Andreas Vesalius[405] in 1562 successfully operated upon Carlos of Aragon for empyema and later reported two other successful operations. Purmann[319] in 1692 likewise advised incision of the chest for this condition. The ancient Japanese and also the Indians of the Great Lakes region are said to have incised with a clam shell knife for drainage of purulent accumulations in the chest, probably empyema necessitatis, and yet in 1835 Dupuytren,[92] the famous French surgeon, allowed himself to die from empyema, saying "he wauld rather die at the hands of God than at the hands of the surgeon."

Drainage and plastic operations for empyema thoracis and its complications constituted the vast majority of thoracic surgical procedures for many years. They were done by general surgeons with good results until the influenza epidemic of the first world war with its streptococcal and staphylococcal exudates changed the picture completely. The appalling mortality which followed the standard drainage operations previously used for pneumococcal effusions led to extensive studies which taught much concerning respiratory physiology and the mechanics of respiration. The report of the Empyema Commission and the monograph of Evarts Graham[138] "Empyema Thoracis" were particularly valuable.

The flood of articles in the surgical literature on special methods and techniques for treatment of empyema did much to confuse the average practitioner in spite of the stabilizing influence of Hedblom,[164] Graham,[140] Harrington[155,157] and others of wide experience in the thoracic surgical field. Most surgeons entering the thoracic field made their first publication on the treatment of empyema. Aspiration, followed by catheter drainage during the acute and sub-acute stage of the effusions, reduced the early mortality and became the standard and most successful treatment. In spite of everything, chronic cases still occurred.

Chronic Empyema

Unrecognized and inadequately drained empyemas and tuberculous empyemas over the years became the bane of the patient's (and the surgeon's) existence. Chronic suppuration, deforming scoliosis, multiple operations and amyloid disease added to the problems. Repeated rib resections usually did not result in cure. Early studies by Simon[373] in 1869, by DeCerenville[78] of Lausanne in 1877, and Estlaender[102] in 1879 were directed at the problem. The thesis of Julien Gourdet[136] of Nantes in 1895 did much to clarify the problem of obliteration of space in the chest in empyema as well as in tuberculosis.

These studies on cadavers were stimulated by an operation for empyema performed by Boiffin[37] in 1894. The very radical, deforming and the shocking Schede[357] flap excision of parietal pleura, intercostal muscles and ribs was often used but even then might not completely eradicate the empyema pocket.

Cornil[64] in 1891 noted that the power of the lung to expand was not lost even when encased in a thick "pleural peel." George R. Fowler[111] in October, 1891, operated upon a patient who had developed empyema following an attack of "Flu." He removed the fibrin mass, apparently freed the lung and excised the external fistula. Delorme[80] in 1893 reported a decortication but the patient died from shock and hemorrhage following surgery. Fowler[111] in 1893 in ignorance of Delorme's previous report first performed a successful decortication with a living patient. Ransohoff[324] noted that in incising the visceral pleural membrane, the underlying lung bulged through the incision on inspiration and carried out his "grid iron" procedure in 1900. Undoubtedly many procedures of many types were carried out over the years but never reported.

Empyema

Howard Lillienthal[245] in 1915 reported a series of 23 patients operated upon early in the course of the disease, incising the visceral peel, thus freeing the lung and the fissures with a 17% mortality. Following the first world war and the Influenza epidemic, Lt. Colonel William Keller[199] at Walter Reed Hospital did an excellent job of clearing up a large number of chronic empyemas, "surgical failures" collected from the armed services, and by many procedures rehabilitated many of them. Samson and Parker[303] in 1945 reported on military experience with infected traumatic hemothorax and showed 19 of 25 primary cures with primary healing. Parker[304] and Burford in 1948 had similar experience.

On the local scene Knute Hoegh[174] of Minneapolis in 1889 operated upon two patients by an Estlaender[102] type of procedure. C. H. Mayo[266] and Emil Beckman of Rochester reported in 1914 two cases treated by visceral pleurectomy done in 1911, and 1912. E. P. Quain[321] of Bismarck in 1920 performed a six-rib thoracoplasty on a seven year old girl with a chronic nontuberculous empyema but could not carry out any decortication because of excessive bleeding. Hedblom[164] in 1920 and Harrington[155] in 1925 reported on the Mayo Clinic' experience with empyema. For many years at the University of Minnesota Hospital Harry Ritchie[330] of St. Paul did excellent work in two very different and difficult fields—chronic empyema and Hare-lip-cleft palate. Wangensteen[417] in 1934-35 also made a report on the University Hospital' experience. The Minneapolis General Hospital and the Sanatoria of Minnesota and the Dakotas[206] provided this author with a considerable volume of nontuberculous and tuberculous empyemas. The clotted fibrinothorax (missed empyema) following antibiotic-treated pneumonias and the unexpandable lung following pneumothorax treatment of pulmonary tuberculosis as well as traumatic hemothorax produced a considerable volume of patients requiring decortication.

Anesthesia

The problem of anesthesia was always of prime importance to the surgeon undertaking thoracic surgery. Ether in adequate concentration obliterated the cough reflex and increased secretions both of which favored the spread and retention of bacterial-containing secretions disseminating tubercle bacilli as well as other infection. Chloroform for longer procedures was potentially quite toxic. Local anesthetics unless very skillfully handled were often unsatisfactory. Nitrous Oxide was a suffocation type of anesthesia and with the attendant cyanosis did not give adequate anesthesia or relaxation. The Carbon Dioxide absorber was added to the gas machines in 1935. The newer anesthetic gasses, Ethylene and cyclopropane, were an improvement and permitted better oxygenation but were explosive.

The intratracheal tube which had been in use since Meltzer[271] and Auer's report of 1909 was supplemented by pharyngeal packing so respiration could be controlled. The intratracheal cuff was introduced by Guedel and Waters[148] of Madison in 1937.

Ether in oil per rectum and Avertin per rectum were used. Evipal by vein for short procedures came in about 1933-34 followed by Sodium Amytal which gave too long a narcosis.

Pentothal Sodium (Thiopentone) was introduced into clinical use by Lundy[257] of the Mayo Clinic and Waters of Madison in 1934 as a more satisfactory agent.

Walter Raleigh in 1595 mentioned the South American Indian arrow poison from which Curare is derived. Arthur Lawen[234] in 1912 used some in an attempt to reduce the amount of ether needed to produce relaxation in abdominal surgery. Griffith[145] and Johnson of Montreal in 1942 used Curare to give relaxation. With the introduction of relaxing agents, Curare, Intercostin and Detubo Curare to intravenous solutions, intravenous anesthesia became available for thoracic surgery.

As the problem of anesthesia became more complex, the need for physicians to take over the work became increasingly apparent. The pioneers Guedel, Beecher, Waters and Cullen stand out. On the Minnesota scene we find the names of Lundy,[250] McCuskey, Tovell, Touhy, Seldon and Matthewsen from the Mayo Clinic,[312] and from the Twin Cities, Knight,[212] Cole, Baird, Friend, Van Bergen, Crowley.[70] Anesthetic machines were developed and improved to aid in control of the various agents and combinations thereof. The Heidbrink of local manufacture and especially the Lundy improvements were of particular value.

Dr. John S. Lundy[312] was brought to the Mayo Clinic by W. J. Mayo from Seattle in 1924 and became the head of the section of anesthesia and developed it to its superb state. Previously anesthesia, usually ether, was administered by specially trained nurses for many years. Dr. Lundy had been preceded from October 1, 1920, to September 29, 1921, by Labat[312] special lecturer in regional anesthesia who was brought over from Paris by Dr. C. H. Mayo for that purpose. His book "Regional Anesthesia"[225] published in 1922 is still a valuable reference book and a treasured volume in any medical library. Lundy[257] in 1929, organized the Anesthetists Travel Club which in 1952 became the Academy of Anesthesiology, the latter word coined by Paul M. Wood of New York. He was delegated in 1933 to take over transfusions in children and later that same year that service for all patients. He began refrigerating citrated blood in 1935 in Dr. W. C. McCarty's pathology laboratory refrigerator and established the first Blood Bank in the country, a year before the Blood Bank was started at Cook County Hospital. This Division was later taken over by Dr. T. H. Seldon[312] and later by Dr. Matthewsen.[312] Under such direction anesthesia for all types of surgery became outstanding and many physicians were trained under their direction.

The Twin Cities had similar problems in anesthesia. Chloroform, then Ether and later Nitrous Oxide, expensive at first and suitable for short periods only, was administered by a nurse or some physician who was free at the time. Robert Emmet Farr[104] an early advocate of local anesthesia performed almost every type of surgery under local anesthesia aided by soft music from a phonograph. His book on "The Techniques of Local Anesthesia" published in 1923 contains much valuable material. His associate, Dr. Stanley Maxeiner[262] carried on the work. The nurse anesthetists did a marvelous job with the drugs and equipment available but worked under handicaps. The early thoracoplasties at Glen Lake Sanatorium started by Dr. Arthur A. Law[131,233] in 1922 were done under intercostal block and light Nitrous Oxide with extreme speed but with much shock and reaction. Soon after I took over the surgery at the Sanatorium in 1928, I was confronted with a severe diabetic patient with a large pulmonary cavity and before Insulin was available, I carried out a three stage thoracoplasty under local infiltration anesthesia and intercostal block in the field with good results and without the patient missing a single meal in the postoperative period. Subsequently all thoracoplasties were done by a similar technique with low mortality and much less blood loss and shock, and a much smoother recovery. In one series of over 1500 stages of thoracoplasty only two transfusions were given.

Dr. Ralph T. Knight,[212] returning from service in World War I, became instructor in surgery at the University under Dr. A. C. Strachauer, following James W. George, a general practitioner who as a part-time instructor had done some teaching about 1920 using chloroform and ether.

Blood pressure recording was introduced in 1923. Nitrous Oxide was used only occasionally because of its high cost. The carbon dioxide absorber was added in 1925 and Ethylene in 1926. Ann Whelan (Arnold) was added to the staff as instructor in August, 1927. Dr. Knight[213] became director of anesthesia for both the University and Minneapolis General Hospitals and their school for nurse anesthetists in 1930. Avertin per rectum was added in 1929-30 and Cyclopropane displaced all others except when cautery was to be used. By 1935 controlled respiration and induced apnea for special situations was added

as suggested by Guedel.[149] During 1933-34 Evipal for short procedures and Sodium Amytal and Sodium Pentothal were used more and more, though much surgery was done under Nitrous Oxide and ether. Spinal anesthesia was administered for many upper abdominal cases using Procain and some Nupercain. Early in 1939 a fatal Cyclopropane explosion occurred at the University Hospital[401] at the termination of a thoracoplasty operation again calling attention to the dangers of using a flammable anesthetic and directing attention to intravenous anesthetics. Intratracheal insufflation as recommended by Meltzer[271] and Auer in 1909 was in common use but for controlled respiration, pharyngeal packing was used in order to obtain a gas seal for positive pressure inflation of the lungs. Waters[148] of Madison re-introduced the inflatable cuff intratracheal tube in 1937. This improvement plus intratracheal suction for removal of secretions were of great help in thoracic surgery. My first three lobectomies for bronchiectasis at the Minneapolis General Hospital, the first in the local area in 1937, were done with nurse anesthetists and without intratracheal tube or suction and why the patients recovered without complications is a mystery.

Knight's[213] first private anesthesia patient was one of mine, a 64-year old man with bronchogenic carcinoma, upon whom we did a right total pneumonectomy, 1937, at Northwestern Hospital,[293] the first successful one in Minnesota. He survived 13 years and nine months, dying from hypertensive cardiovascular disease without recurrence of carcinoma. We engaged Dr. Knight for every chest case from then on. His school for anesthesiologists and accessory school for anesthetists developed as he added to his staff. Dr. Cole[212] first joined the staff and Dr. Baird, then Dr. William Friend and later others. As his staff grew he extended anesthesia coverage to Ancker and Miller Hospitals in St. Paul, St. Mary's and Veterans Hospitals, Northwestern and Deaconess in Minneapolis. Dr. Cole left the group in 1943 for St. Mary's Hospital in Duluth to become the first Anesthesiologist in the state outside of Rochester and the Twin Cities. By 1946 there were under Dr. Fred Van Bergen[213] 18 residents in anesthetic training at the University and affiliated hospitals. Gradually the general surgeons who at first were reluctant to use physician-administered anesthesia recognized the importance of it to the extent that now the large hospitals may have as many as six to seven anesthesiologists busy at all times. Dr. Knight retired in 1954. Dr. James H. Crowley,[70] a Rochester-trained anesthesiologist, took charge at St. Joseph's Hospital, St. Paul, in 1948 and has continued to date.

Without the pioneering efforts of Lundy, Knight and Crowley, thoracic and cardiovascular surgery in Minnesota could not have developed as they have and general surgery owes an equal debt to these men. As the thoracic operations became more extensive and complex, and cardiovascular procedures and open heart and transplant operations came into the field, the duties of the anesthesiologist became more demanding.

Intratracheal Tube

Robinson[332,333] and Brauer in 1908 showed experimentally that under a steady air flow with both pleural cavities open and no lung motion, surgery could be carried out for two to four hours but there was a carbon dioxide build-up. Meltzer[271] in 1909 demonstrated that the lung could be aerated through an intratracheal tube with escape of air along side the tube with no lung motion. Robinson[337] in 1912 developed an apparatus with positive pressure for intratracheal anesthesia with ether by closed mask without the tube and also via intrapharyngeal, intrabuccal and intratracheal administration. He moved to Europe in 1913 to work with Sauerbruch in thoracic and experimental surgery. He returned to the United States to the Mayo Clinic[312] in 1915, to become head of the newly created section of Thoracic Surgery.

Karl Connell in 1912 advocated pharyngeal insufflation, a method adapted to thoracic surgery by Branower in 1913. The carbon dioxide absorber was added to the gas machines in 1925. Induced apnea was introduced in 1935 by Guedel.[148] The cuffed intratracheal tube was introduced by Waters[148] of Madison, Wisconsin, in 1937, enabling the anesthesiologists to better control the anesthesia and lung secretions. The cuffed tubes were not commercially available for some time. The homemade version with a somewhat more rigid cuff was responsible for the loss of a child who had a lower lobe lobectomy for bronchiectasis in 1939. A local slough of the tracheal mucosa from unrelieved pressure and

death from suffocation followed.

The value of the intratracheal tube is well illustrated by two of our early surgical patients. The first was a 20-year-old girl with extensive unilateral bronchiectasis since childhood, from whose trachea Knight aspirated well over a liter of pus during a pneumonectomy.[351] The second was a man who had profuse pulmonary bleeding from a metastatic synovioma in the lung pouring out over 750 cc of blood into his trachea in the time it took to open his chest and clamp the lower lobe bronchus.

The double lumen catheter of Carlens,[47] Gebauer[124] and others for bronchospirometry not only allows selective pulmonary function studies but affords better control of respiration in patients with profuse secretions or hemorrhage, or situations requiring bronchial plastic or transplantation procedures.

Pressure Chamber - Intratracheal Anesthesia

Ferdinand Sauerbruch[275] became assistant to Von Mikulicz at Breslau in 1903. By 1904 he had developed a negative pressure chamber for experimental work on dogs. The first chamber would accommodate two persons for surgery but within two hours the temperature within it became too hot for comfort. Later the chamber was enlarged with 14 cubic meters of air and would permit five people to work within it. Sauerbruch, sponsored by Von Mikulicz in 1904 demonstrated this chamber before the German Surgical Society, reporting that they had performed thoracic operation on 78 dogs without mortality using a negative pressure of 10 mm of mercury. Dr. H. Willy Meyer[273] of New York visited Breslau later in 1904 and was privileged to observe the surgery—a transthoracic resection of the esophagus on a dog. Resections of the esophagus were later carried out on 10 dogs in a larger chamber. The first human operated upon for a carcinoma of the esophagus in the larger chamber died during the procedure. The next patient survived the removal of the mediastinal tumor. A number of positive pressure cabinets were developed in Europe. Brauer[275] of Heidelberg developed a mask-type but preferred the negative pressure type. Robin, Matas and others overcame the tendency for the lung to collapse when the chest was opened by blowing air into the trachea. Von Mikulicz died of cancer in 1905 and was followed at Breslau by Prof. Garre. Sauerbruch was then transferred to Greifswald under Dr. Friedrich. They moved to Marberg in 1907 and there continued their experiments.

Sauerbruch appeared before the Surgical Section of the American Medical Association in Chicago in 1908, reading a paper and demonstrating his negative pressure chamber. He was the guest of Dr. Herbert Willy Meyer[275] and after the meeting returned to New York with him, presenting the chamber to Dr. Meyer. It was installed in the Rockefeller Institute, where he operated upon a dog with Dr. Meyer assisting. By the fall of 1908, Dr. Meyer and his brother, a mechanical engineer who had studied all of the available machines in Europe constructed a larger chamber for both positive and negative pressure use. Subsequently another and much larger commercial chamber was built in May, 1909, and used experimentally and clinically until 1923. With the development of closed-mask and intratracheal anesthesia, the negative pressure cabinet was no longer needed and so was abandoned for clinical surgery.

Blood Bank

The first transfusion (Hoff[175]) for a human being is reported to have occurred in Paris in 1667. An edict from the Criminal Court of Paris was issued in 1668, forbidding further transfusions in man until approved by the Faculty of Medicine of Paris. Lower[175] of Oxford, apparently was the first to conduct experimental transfusions in animals in 1665 replacing the blood removed with equal volume of beer and wine and later blood from another dog. The experimental work of Denis[175] and Emmerez of Paris in March, 1667, included dog-to-dog transfusion, calf-to-dog, sheep-to-boy and sheep-to-man without difficulty. One man received two transfusions without reaction but died the next day. A hemiplegic woman also a mental case received two transfusions and apparently improved. Apparently no human-to-human transfusions were done.

The importance of available blood for transfusion cannot be over-emphasized when many thoracic surgical procedures are to be undertaken. The blood loss can be considerable and unavoidable, adequate replacement is mandatory. Sporadic attempts at blood transfusion occurred for many years, often with disastrous results. Landsteiner in 1900 grouped patients and donors, thereby reducing the risk of reaction. Hustin[175]

of Belgium in 1914 introduced the use of citrate and glucose for transfusion. Robertson[175] of England in 1918 was the first to preserve citrated blood. Transfusions were not then commonly used. As an intern at Minneapolis General Hospital in 1919-1920, I well remember direct transfusion by syringe transfer and indirect by the use of the paraffin tube method. Later relatives and friends were held around to be bled as the occasion arose. There came a time when it was positively dangerous for friends and relatives to visit a patient at the University Hospital for they were sure to be captured and bled. Walking blood banks were organized in many communities among the police and firemen, lodge members and civic groups for emergency use. Lundy[257] of the Mayo Clinic began to store citrated blood in McCarty's pathology laboratory refrigerator at St. Mary's Hospital, Rochester, in 1935, thus establishing the first Blood Bank a full year before the Cook County Hospital Bank was established. The Rochester walking blood bank had been in use for many years on a pay-for-donation basis, one man setting a world record of 214 donations over a period of 36 years.

Locally before undertaking an extensive intrathoracic surgical procedure, it was necessary to have a half dozen suitable donors at hand before starting the operation or have them bled immediately before starting. I vividly recall in 1939 at Abbott Hospital undertaking the removal of a huge intrathoracic neurofibroma which proved to be very adherent, with severe blood loss. When we had given four units of blood it became evident that we could not complete the excision with the two units of blood still available. The field was packed and a call sent to the patient's brother who was a captain of police. Within minutes we had a dozen husky policemen, group IV donors, at the hospital. The resection was completed without incident: the patient recovered.

Our problem at St. Mary's Hospital,[351] Minneapolis, was complicated by the fact that many of our patients were from out of town, many from the Dakotas, Montana, and Wyoming.

This problem was met by having the referring physician cross-match the patient and relatives and friends, and then bleed six suitable donors and send the six bottles in ice down with the patient two days before the scheduled operation with two vials of blood attached to each bottle, so our laboratory could carefully recheck each unit with the patient before using it. We were careful to explain beforehand that any excess blood not given to the patient would be placed in a pool to be used in emergencies and for Indians and county patients who could not furnish their own. In this way there were times when we had as much as 20-30 unit credits in the refrigerator, but it was usually used up promptly by the numerous Indians we were operating on for the Indian Bureau and the State Sanatoria of Minnesota and the Dakotas. St. Mary's Hospital, Minneapolis, established its own Blood Bank[351] in 1943 under Dr. R. Koucky, our pathologist. This permitted us to transfer patients from other local hospitals which did not have their own banks.

Minneapolis through the Junior Chamber of Commerce organized the City-wide Blood Bank in 1946 on a small scale. The War Memorial Blood Bank[277] began in 1948, simplifying our problems very materially. The development of the Rochester Blood Bank must be credited to Mathieson[312] while the War Memorial Bank, Minneapolis, is to the credit of Matson.[260] In 1961 in Rochester 21,000 units of bloods were processed and over 36,000 units in 1965 in Minneapolis. The growing cardiac surgery load will probably increase this materially. The Minneapolis Bank[277] in 1967 processed just under 45,000 units.

Clinical Laboratories

The early laboratory studies for chest surgery in the twenties were quite minimal. Blood and urine examinations were usually sufficient for most cases with a few additional studies in special circumstances. As the surgical procedures became more extensive and more complicated, as additional diseases and conditions were accepted for surgical relief, and older and more debilitated patients subjected to operation, much greater demands were made on the laboratories for help and guidance in the treatment. A simple hemoglobin, white count and differential were inadequate. Special cell type studies, reticulocyte count, iron studies, cross-matching including the minor groups, Rh factors and sensitivity, blood metabolites and electrolytes, blood gasses, antibiotic levels, and a host of others became available and were used extensively. The electrocardiogram is no longer three leads but

multiple tracings with exercise and various stress factors added. The single total vital capacity no longer suffice, but timed studies, rates and other factors are studied. Sputum smears alone are not enough but cultures, sensitivities to antibiotics, cell studies for malignant cells are needed. Radioisotope studies, liver and kidney function studies are all available to aid the physician and surgeon. They help the physician but at the expense of the patient, for the laboratory bills are frequently appalling. Automation has helped some with batteries of tests done at little added cost, but the teaching methods today which require a complete survey of everything on every patient has contributed much to the skyrocketing cost of medical and hospital care. Tools can be used but they are often abused.

The clinical pathologist has developed and expanded with his domain and has been alerted to new techniques added to his laboratory. In the thirties our one pathologist at St. Mary's could cover everything, and during the war years covered three other hospitals in addition. Now with three full-time men, they are busy all the time. Without the guidance of these men, thoracic surgery and other specialties could not have functioned and developed to their greatest potential.

Xray

Without a doubt the single most valuable tool available for discovering, diagnosing and guiding the treatment of chest disease has been the Xray. Some consideration of its discovery[233] and development seems necessary in any history. Geissler[129,144] in 1858-59 made the first vacuum tube. Hettorf in 1860 noted that the luminous stream —cathode rays—from this tube was deflected by a magnet. The work of these two was followed by the experiments of Crookes[67] with a higher vacuum tube. The glow disappeared and these rays were intercepted by a metal plate. Hertz[233] in 1892 noted that the rays penetrated thin gold leaf and other thin metal. When he died, the experiments were carried on by Prof. Lenard.[233] The rays penetrated many substances and would excite fluorescence from barium platino cyanide and other substances. In 1895 W. K. Rontgen,[129,344] Professor of Physics at the University of Wurzberg, Austria, noted that paper coated with barium platino cyanide fluorescenced brightly even though the tube was cardboard-covered. The rays could not be deflected or refracted and were much stronger than the cathode rays. He experimented with photographic plates wrapped in paper and produced pictures of metal objects and the bones of the hand. When presenting this finding at the December, 1895, meeting of the Wurzberg Physio-Medical Society he claimed that he had discovered a new kind of ray which he called "X" for the unknown.

Rontgen's discovery of Xrays became one of the most important factors in the diagnosis and treatment of disease of the chest. Potain[283] in 1897, in Paris, before the Academy of Sciences demonstrated pictures which were purported to be the first two pictures of the chest made by Xrays.

Pupin[283] in 1896 made the first radiographs of the chest in the United States, placing a fluorescent screen between the patient and the photographic plate. John B. Murphy[283] in his presidential address to the American Medical Association Meeting at Denver in 1898 showed x-ray pictures of the chest. Mach and Thomson[144] in April, 1896, first used the steroscopic technique in radiography. Bleyer, Battelli and McIntyre[144] in July, 1896, first used the photo fluoroscope. Bucky[129] developed his grid in 1915 to be improved by Potter in 1919 as the Potter-Bucky diaphragm. The principles of body section radiography were first outlined by Bacage[129,144] between 1917 and 1921. Vallebona[129,144] in 1930 reported his technique which he called stratigraphy. There followed other techniques called planigraphy by Ziedses des Plaines[129] in 1931, Tomography by Grossman[130] in 1935, and Laminography by Kieffer[130] in 1938.

Sicard and Forestier[372] reported making bronchograms with lipiodol in 1922. Berberich and Hirsch[129] in 1923 reported the first arteriogram and venogram in man using 20% Strontium bromide. Forssman[110,129] in 1926 catheterized his own heart. Moniz, Calvalho and Lima[130] in 1931 demonstrated the pulmonary vessels in man with sodium iodide. Castellanos, Pereiras and Garcia reported the first roentgen contrast demonstration of congenital cardiac abnormalities in 1937.

Goodspeed[134] from the Physics Laboratories of the University of Pennsylvania accidentally made an x-ray photograph on February 22, 1890, six years before Rontgen's discover, but claimed no credit for the discovery. Morton[233] of New York was the first to produce a photo with the Holtz

machine in which the static-induced current from a Rhumkorf coil is coupled to the tube and outer coating of a Leyden jar and regularly interrupted by a system of rods.

Two months after Rontgen reported on his development of the Xray, Dr. John Grosvenor Cross,[69] an independent practitioner in Rochester, Minnesota, bought an x-ray machine for his office in February, 1896. He demonstrated its used before the Southern Minnesota Medical Society in August, 1896, and in 1897 before the Olmsted and Wabasha County Medical Societies. Blake[406] of Kansas made an x-ray picture of his hand on February 11, 1896.

The rapidity with which Xray was accepted about the country is illustrated by a news item in 1896, which reported that in an Iowa[433] suit for malpractice in a fracture case, the trial was postponed until Xrays were obtained. Surgeons were prompt to recognize the value of this new tool and to use it in their practice, notably Dr. A. A. Law and Dr. Geist in Minneapolis, Drs. Arnold Schwyzer and H. J. O'Brien at St. Joseph's Hospital in St. Paul, and Dr. Arthur Colvin at City and County Hospital and later at St. Luke's in St. Paul.

C. H. Mayo[264] in January, 1897, brought to Cross a small boy who had swallowed a vest buckle. Two skiagraphs were made by a twenty-minute exposure, demonstrating the buckle in the cervical esophagus, from which it was removed through a cervical esophagotomy by Dr. Charlie Mayo.[264] During the next three years, Cross did considerable work for the Mayos for fractures and foreign bodies. Soon he was receiving referred patients from the Twin Cities. He sold his practice to Dr. Crewe[60] of Rochester and then spent two years in study in Vienna in internal medicine and upon his return, moved to Minneapolis in 1902. His thesis for admission to the Minnesota Academy of Medicine in 1901, was entitled "Present Status of Xray in Medicine and Surgery." We can find no reports of x-ray work by Dr. Cross in Minneapolis where he was an internist and on the Medical School Faculty.

The Mayos purchased an improved type of x-ray machine in 1900. This model was also equipped with flashing lights and jumping sparks which did not appeal to Dr. Will, who soon had these outlets plugged with wooded pegs. Dr. Charlie[60] did considerable work with it and sustained injuries to his fingers in the process. Dr. Christopher Graham[60] later was in charge as part of the laboratory section and made attempts to study chest and other organs.

The first local diagnosis of carcinoma of the stomach by x-ray means was made at the Mayo Clinic in 1909 by Willey, working with Plummer, who also sustained x-ray injury to his hands. The department did not come into its own until Dr. Russell D. Carman[312] took over in January, 1913. Dr. Charles G. Sutherland[312] became first assistant in radiology October 1, 1918, and Dr. Alexander Moore[312] became head of the section in 1926 upon Dr. Carman's death. Dr. Byrl R. Kirklin[312] became head of the section in January, 1930. Harry M. Weber[312] was first assistant in roentgenology and associate in 1931. Leda J. Stacy was the head of the Radium therapy in 1915 succeeded by Harry Bowing[312] in 1919.

Drs. Stephen A. Kiefer and Eugene Gedgaudas, reporting on the history of the Department of Radiology of the University of Minnesota in Myers'[285] "Masters of Medicine," noted that within six months of Rontgen's report of the discovery of Xrays, the University student newspaper "Ariel" reported that "Professor F. S. Jones' new Fluoroscope and Crookes tube had arrived and both proved to be all that was expected," and later on October 24, 1896, reported that Professor Jones, of the Department of Physics of the University of Minnesota, on October 23 at the request of Dean Millard had at the City Hospital in St. Paul located bullets in the legs of two patients with the aid of an x-ray machine. It also notes that he had made an x-ray photograph of a hand with a five-minute exposure. These pictures are not the first in the Twin Cities for Dr. Law[233] had demonstrated a number of x-ray photographs before the Minnesota State Medical Society meeting of June 18, 1896.

Xrays in Minneapolis

Dr. Arthur Ayer Law,[233] then associated with Dr. Frederick A. Dunsmoor, the outstanding surgeon of the city, on June 18, 1896, before the Minnesota State Medical Society delivered a paper entitled "The Xrays," in which he discussed the origin of the discovery and its development, and demonstrated some skiagraphs which he had made, and listed some of its possibilities. He reported having made skiagraphs of needles, pieces of glass, bullets, even through the chest,

fracture callous, and tuberculosis of the os calcis, tumors of the extremities and uric acid deposits. He used both the fluoroscope and skiagraph and noted that cholesterol gallstones and oxalate kidney and bladder stones cast little shadow which precluded their being so diagnosed. Phosphatic stones were more resistant to the ray and uric acid the most resistant. Early exposures varied from 15 minutes to two hours. This paper was published as the lead article in the *Northwest Lancet,* 17:6-8, 1897. His second paper given before the Minnesota State Medical Association Meeting on June 18, 1897 appeared in the same volume.[232] He reported on 15 months of experimentation without ill effects on himself. (This would mean he had a machine at least by March, 1896). He discussed the many improvements in equipment since originally introduced with exposures reduced to three to ten minutes. His early work was done with a large Holtz machine but later with the Tesla addition.

Arthur Law in a letter dated September 18, 1898, from the Philippines[119] wrote: "We are short of Doctors—every man already has charge of from 60-80 sick. The hospital is fairly well supplied with most of the necessities. A large x-ray machine is here and is my special charge."

For many years Law maintained x-ray equipment in his and Dunsmoor's office for his own use. A staff list of Asbury Hospital for 1904 listed Dr. A. A. Law for Xray and surgery.[308]

Dr. Charles D. Harrington[154] had a Noth x-ray coil machine in 1897. He loaned the coil to St. Barnabas Hospital, the oldest hospital in the city in 1899. Northwestern Hospital also added equipment in 1899.

Dr. Charles A. Erdman[101] in 1900 published an extensive study of the anatomy and mechanisms of the wrist joint. The x-ray pictures were of his own wrist made by D. C. Cole, then a medical student at the University.

Dr. Ray Knight[214] and Dr. Woodward had had a static machine since 1909. They added an 18-inch coil in 1910-11 and in 1913 added the first advanced Snook apparatus in Minneapolis which subsequently was sold to the Medical School to start the Xray Department. It was later turned over to the Dental School where it was used until 1949. The radiologists of the period were: Harrington, Spring, Donaldson and later Bissell.

Robert G. Allison[8] came to Minneapolis in 1920 as Assistant Professor of Radiology at the University and opened a private office for radiology. He had been in radiology at Trudeau Sanatorium, at Cornell University and under Col. Lewis G. Cole of New York. He had been radiologist at Harper Hospital in Detroit and the Municipal Tuberculosis Sanatorium in Chicago. While in charge at the University, the George Chase Christian Memorial donation to the Cancer Institute provided 200 mgms of Radium in tubes, one half gram of Radium in solution for the Radon plant and a 200 K.V. x-ray therapy unit. This later was permitted to remain idle and unused until Dr. K. W. Stenstrom arrived in June, 1926, and took over the radiation section. The two sections were separated in 1937 with Dr. Leo G. Rigler in charge of Radiology. A second high voltage 400 K.V. therapy machine was added in 1942 as another gift from Mrs. Christian. Mrs. Archie Walker in April, 1953, donated a 1,000 Curie Cobalt 60 therapy installation, the second unit of its type in the United States.

The Xray Department at St. Barnabas Hospital for a three-month period in 1903 reported expenses of $18 and an income of $84. As late as 1916, the total income of the department was $2,200.

Early Thoracic Surgery in the Twin Cities

When this author left full-time work at Glen Lake Sanatorium in September, 1936, for private practice in Minneapolis, there was no established field of Thoracic Surgery. The volume of work available was small, consisting of surgery for empyema, for tuberculosis and administration of Pneumothorax. Even the Mayo Clinic did not have sufficient volume of chest surgery to keep one surgeon busy. The field was expanded by a slow gradual process of development of techniques, instruments, and methods of handling and care. As the lone surgeon with interests along this line in the city and wide surrounding territory, there were times when it was not unusual to have patients in seven or eight different hospitals at one time, requiring much traveling for hospital calls and dressings and much transporting of all special instruments and equipment. It was not until after the end of World War II that training programs in surgery produced men interested in this field and trained in chest work that others entered the local practice of chest surgery. Gradually a number of well qualified men entered the field which now is well covered:

Drs. N. K. Jensen, W. R. Schmidt, Frank E. Johnson, Joseph A. Garamella, Michael F. Lynch, Aydin M. Bilgutay, William D. Kelly, Paul Gannon, Charles A. Peterson, Theodore A. Peterson, Jerome T. Grismer, Richard E. Larson.

In St. Paul Dr. D. Greth Gardner was the pioneer following Dr. Lou Daugherty, then Drs. N. Logan Leven, Lyle Tongen, Bernard G. Lannin, Samuel W. Hunter, Bernard Goott and Coleman J. Connolly.

American Association for Thoracic Surgery

The American Association for Thoracic Surgery was founded in New York in 1917, as an outgrowth of the recently organized New York Society for Thoracic Surgery, which was the first such Society in the World. Willy Meyer had sensed the necessity of bringing together a group of men interested in problems of thoracic disease and the need for a place to discuss the many problems of this infant surgical specialty. Membership was not limited to surgeons but included allied specialties related to thoracic problems including allied specialties related to thoracic problcluding: Internists, Phthisiologists, Endoscopists, Roentgenologists and Pathologists. The Charter Member Group of fifty names was widely distributed but contained five from Minnesota: Dr. J. Frank Corbett and Dr. A. A. Law of Minneapolis, Dr. William Lerche of St. Paul, Dr. Walter Boothby and Dr. Samuel Robinson of Rochester. Another Dr. Kenneth Bulkley who was the original secretary of the New York Society later moved to Minneapolis and became associated with Dr. Law in October, 1921. Within the next year, three more Minnesotans were added—Dr. Henry S. Plummer, Dr. Frank C. Mann and Dr. Carl A. Hedblom, all of Rochester.

From this group Dr. Corbett did no chest surgery except for empyema unless it might have been in service, his interests being in experimental work and later in Neurological surgery. Dr. William Lerche was primarily interested in bronchoscopy and esophageal work though he did operate for mediastinal abscess and esophageal perforations. Dr. Walter Boothby was not a surgeon, but did much work on metabolism and oxygen therapy with the B. L. B. (Boothby Lovelace Bulbulian) mask for aviation and clinical use. Bulkley after coming to Minneapolis assisted Law for a time but did little chest work. Henry Plummer was an internist, interested in esophageal disease and contributed much to the diagnosis and treatment of conditions affecting it. Frank Mann was an experimental physiologist and surgeon. He was a superb surgical technician and through the Institute at Rochester which he headed, taught many of the staff and fellows the intricate techniques necessary in their various problems. Drs. Law, Robinson and Hedblom were clinical surgeons and all three pioneered in the thoracic field.

Under the editorship of Dr. Evarts Graham, the *Journal of Thoracic Surgery* appeared in 1931 as an independent Journal published by C. V. Mosby of St. Louis, later changing its title to *The Journal of Thoracic and Cardiovascular Surgery*.

The Board of Thoracic Surgery was founded in 1948 as a subsidiary to the American Board of Surgery in order to certify the men experienced in surgical disease of the chest. To provide a meeting forum for many of these young men, the Society of Thoracic Surgeons was founded in 1964. Many other papers on chest surgery are to be found in the *American Review of Tuberculosis and Respiratory Diseases and Diseases of the Chest and the British Journal-Thorax*.

Bronchiectasis

Bronchiectasis, bronchiectatic abscess and true pulmonary abscess were not sharply differentiated in the earlier literature. The clinical picture of extensive chronic bronchiectasis was easily recognized but the earlier stages were not even with x-ray studies. Bronchoscopy was of some help. Attempts at bronchial visualization with opaque powders such as bismuth were not too successful. It was not until 1932 when Sicard[372] and Forester brought out iodized oil (Lipiodol) that good visualization of the bronchial tree was accomplished, and the exact extent of involvement demonstrated. Medical management, postural drainage, cough mixtures, vaccines and climatic change often helped temporarily. Instillation of iodized oil at times gave some help. Later antibiotics did help materially as did nebulized antibiotics to control infection during acute exacerbation but did not remove the dilated bronchi or prevent complications. For many years surgery had sought a cure for the condition. Between 1837 and 1880 Richards, Forde, Hall and Grinnell each reported a case of excision of a herniated portion of lung through a chest wall with recovery. Gluck[283]

Sehmidt, Block[283] and Biondi[30] and others in 1885 showed that partial resection of the lung was possible in animals. Heidenhain[169] in 1898 successfully removed a left lower lobe for bronchiectasis and recorded two previous operations for drainage of bronchiectasis with rib resection. Doyen[89] in 1898 successfully removed the remains of a right lower lobe previously drained for a hydatid cyst. Dr. C. H. Mayo[265] in 1898 reported three cases of pneumonotomy with two deaths and one recovery. Krause[217] in 1899 did a partial lobectomy with recovery.

Lung resection continued to carry a very high mortality. Samuel Robinson[332] and others experimentally proved in dogs that lobes of the lung could be removed with a high degree of success. The dog's lungs were not infected while the lungs of patients subjected to resection were badly diseased. As late as 1916, Dr. Robinson[340] made the statement: "Let no man attempt a lobe excision in a single operation in man." Even when done in stages there was a very substantial mortality.

In spite of many disappointments a few brave pioneers persisted in their efforts to relieve patients of this "loathsome" disease. W. Meyer,[274] Lillienthal, Robinson and others struggled to find the answer. Meyer[274] in 1914 reported a 50% mortality in 16 pneumonectomies. Robinson[336] in 1917 recorded one death in five lobectomies done in one to three stages. Lillienthal[248] by 1922 reported a 42% death rate in 14 lobectomies by mass ligation technique. Graham[137] in 1923 introduced his Cautery "Lobectomy" drainage for bronchiectasis reporting a 20% mortality in 20 patients.

Quencke[322] in 1888 and 1896 successfully carried out extrapleural thoracoplasty for bronchiectasis with good effect. Spengler[41] in 1890 advocated the same. DeQuervain[83] advised lobectomy after thoracoplasty. Mumford and Robinson[336] did three lobectomies after thoracoplasty, losing two. Meyer[274] in 1914 reported 16 lobectomies with eight deaths. Robinson[338] in 1917 reported a series of five lobectomies with one death. Four of the patients by operative dates and registration numbers were Mayo Clinic patients and Robinson, a Mayo Clinic surgeon. The fifth patient also his was from Massachusetts General Hospital. Robinson therefore must receive credit for introducing lobectomy for bronchiectasis to Minnesota. Harrington followed in 1931[158] and 1936.[159] Saurbrueh[355] in 1920 reported three single stage resections with three deaths. Lillienthal[248] in 1922 reported 21 cases with 12 deaths and seven recoveries. Graham[137] in 1923 reported three cases with two recoveries. Hedblom[167] from the Mayo Clinic reported on 48 cases using graded thoracoplasty in 18 with good results. Nissen[291] in 1931 operated upon a 12-year-old girl in stages mobilizing the upper lobe, pulling it out through the chest wall, amputating it later and following with thoracoplasty. Harrington[158] from Rochester in 1931 reported on 111 patients with 47 pulmonary abscess and chronic suppuration in 64 using thoracoplasty in 31 with good results and only three deaths, lobectomy in four with two deaths and partial resection on nine with four deaths. He[159] reported a right lower lobe resection by the tourniquet technique with recovery in 1936.

Cameron Haight[150] of Ann Arbor did the first successful pneumonectomy for bronchiectasis in the United States in 1932. Nissen[291] of Berlin in 1931 had done a two stage mass ligation of the hilum allowing the lung to slough on the eighth day. Sauerbruch[356] in 1923 in removing a very large ganglioneuroma had injured the blood supply of the lung which necrosed and sloughed, a thoracoplasty was done. The patient recovered. There was no bronchial fistula.

With improved technique and the use of individual ligation of the hilar structures and better understanding of the segmental anatomy of the lung the risks became less. Individual ligation of the hilar structures was used by H. Morrison Davies[76] of England in carcinoma of the lung in 1912. The Jackson[181] and Huber classification of the pulmonary segments and the anatomical work of Boyden[38] did much to develop this technique. Used by Churchill in 1931, by Blades and Kent[200] in 1940 and Overholt[301] in 1941, this became the method of choice and reduced the mortality.

The old warning of Robinson:[339] "Let no man dare to excise a lobe of the lung in a single stage" became obsolete and single stage resections became the rule. Chest suction postoperatively and later antibiotics reduced the mortality very drastically.

Our first attempts to control bronchiectasis began in 1928, when we explored the chest of a young girl with a severe right lower lobe putrid bronchiectasis of years standing with repeated

pulmonary hemorrhage. The plan was to mobilize the lower lobe, deliver and fix it in the posterior incision to be clamped and excised at a later date after adhesions had formed to wall off the pleural cavity. Unfortunately the lobe was so densely adherent to the diaphragm and pericardium that it could not be freed without tearing into the adjacent bronchiectatic abscesses. On December 7, 1928 the adherent lower lobe was exposed and a Graham Cautery drainage carried out. This was well tolerated; with external drainage the symptoms improved, but there was still considerable cough and expectoration. Bronchograms revealed additional involved areas. Additional cautery was done in 1929 and 1930, being very cautious not to do too much close to important structures. The patient improved considerably in spite of the daily routine of dressings. Bronchograms revealed only one segment still involved. She died of respiratory obstruction in 1931 with no residual bronchiectasis.

The second Graham cautery patient, a young man, was done at the University Hospital without incident. He died five days after the operation from hemorrhage from his wound. The next two who had pulmonary tuberculosis also were done with good results, becoming sputum negative and symptom-free. The first survived 20 years, dying from hypertensive disease, the other is still alive and working some 30 years later. A few more were done subsequently without mortality.

Our first one-stage surgical excision in the Twin Cities was done on a four-year-old boy at Minneapolis General Hospital[278] using a tourniquet ligation technique in 1937. He is in good health today. Postoperative empyema was frequent following this technique. Individual ligation soon replaced the tourniquet with fewer complications. We did a left total pneumonectomy[351] in 1937 on a 19-year-old girl who had had bronchiectasis since infancy. More than 20 sputum smears and three guinea pig innoculations had been negative for tuberculosis. The operation was long and difficult with over 1,000 cc of sputum being aspirated from the trachea by Dr. Knight during the procedure which withal was well tolerated. She died six weeks later from disseminated tuberculosis. The excised lung showed much tuberculous disease in spite of the negative findings. The early surgery was without the benefit of antibiotics and the first few without physician anesthesia.

We pioneered resection surgery in Northern Minnesota in 1938, doing a lobectomy for Nopeming Sanatorium[292] near Duluth and a pneumonectomy for Middle River Sanatorium in 1940. Later Jensen and Schmidt took over. Later in Duluth Dr. William Seybold[118] and Dr. John Kirklin[118] from the Mayo Clinic came up to do the work until Dr. Josiah Fuller,[118] a Rochester-trained thoracic surgeon, established practice in 1953.

With the development of intrathoracic surgery, it became necessary to devise equipment to evacuate fluid and air from the pleural space and to maintain expansion of the lung postoperatively. This led to our developing at the Minneapolis General Hospital a suction machine with controlled negative pressure with the suction maintained by a filter pump on a water faucet. Later at Glen Lake Sanatorium with the cooperation of the chief engineer, C. S. Sampson, the suction was provided by the vacuum line of the central heating system. Later the Stedman electric pump was incorporated into the machine, making a portable and compact apparatus. Dr. Robert Glover[132] in 1945, who had spent three months with us at Glen Lake while on his residency at the Mayo Foundation, modified this apparatus which later at the Clinic became known as the Glover suction.

Later at St. Mary's hospital, Minneapolis we became concerned by the occasional local failure of electrical power with the loss of suction or a broken connection or leaking tube between the patient and the machine. With the aid of Oliver Moe, a local instrument maker in 1951-52, we devised a safety valve interposed in the circuit to prevent loss of intrapleural negative pressure. This device, built on the principle of the Thiersch Flapper valve for empyema drainage or the valve used in the Momson escape lung for submarine rescue work, was simple and disposable. It was a check valve made of a small glass cylinder in which a six-inch length of thin penrose tubing was suspended with or without a Z-shaped wire frame to angulate the tubing. By experiment it was found that this check valve could hold a negative pressure of 30 cm. of water for as long as 12 hours with the vacuum pump turned off. We have used this device on all cases for more than 15 years very satisfactorily. Recently a commercial device of similar type has appeared on the market.

There was a considerable backlog of bronchiectasis built up over the years so that for a time after we started resection for this disease, we did a fair number of lobectomies for this condition. Up to the early fifties we saw a fairly steady volume of these cases, but after that it fell off rather steadily as the backlog was cleared up. The experience and technique gained in handling these cases stood us in good stead when resections for tuberculosis came into the picture. In later years in Minneapolis, Dr. N. K. Jensen, Dr. W. Robert Schmidt, Dr. Joseph Garamella, Dr. Frank Johnson, Dr. J. Grismer and Dr. Richard Larson in Minneapolis and Dr. Logan Leven, Dr. Coleman Connolly, Dr. Lyle Tongen and Dr. Sam Hunter in St. Paul did this type of work. With time, antibiotics, better treatment of infectious diseases and pneumonia, and better anesthesia for tonsillectomy, the incidence of this condition has dropped to a new low.

Pulmonary Abscess

Pulmonary abscess and pulmonary gangrene had been recognized as extremely serious conditions which before the days of chemotherapy carried the highest mortality of any disease of the chest with the exception of carcinoma. The differentiation of true pulmonary abscess and bronchiectatic abscess was not clear in the earlier recorded cases.

Politeau[316] and Dared in 1783 advised incision to the pleura and trocar-cannula insertion to the depth of the pus. Faye[316] in 1797 operated for adherent abscess punctured, opened, irrigated, and tamponed the cavity. Jaymes and Richerand[316]in 1813 also advised incision and drainage. Callisen[45] in 1815 advised puncture paracentesis and if pus was found, incision to the fluid area. Brichatan[316] in 1830 opened the area with caustic paste and incised the abscess. The patient lived nine months. Before the Minnesota State Medical Society, Dr. Christian Fenger[106] of Chicago in 1881 described open drainage of pulmonary cavities, quoting four cases successfully treated by open drainage, making counter drainage in one which proved to be an echinococcus cyst whose wall he removed by finger dissection. Murphy[283] in his Presidential address to the American Medical Association in 1898 mentions trocar drainage. Dr. C. H. Mayo[265] reported in 1898 on pneumonotomy for pulmonary abscess on three patients with two deaths and one recovery. Frankel in Germany in 1899 reports that 5% of "Flu" pneumonias ended in gangrene.

Emile Holman[176] in 1926 proved experimentally that pulmonary abscess could be produced by septic emboli. Smith[376] in 1927 produced pulmonary abscess by the intrabronchial injection of pus. This emphasizes the importance of the cough reflex in protecting the lung from aspirated material. Clinically the average abscess seen is the result of aspiration of material or foreign body in a submerged or unconscious patient rather than an embolic process for the usual embolus is a sterile clot rather than a septic one. Lambert[227] and Weeks in 1929 emphasized the role of the anaerobes in abscess formation. Neuhof and Tourof[288] in 1936 recommended the two-stage drainage of putrid abscess. Kent in 1947 advocated resection for treatment.

Many other isolated case reports may be found, but in spite of some favorable results Graham[137] in 1923 collected 48 cases with a 52% mortality. Wangensteen[418] described his graded cannula-cautery technique for drainage in 1937.

Pulmonary abscess is a complication of tonsillectomy under general anesthesia, aspirated foreign body, vomiting in an unconscious or obtunded patient, head injury and cerebrovascular accident, particularly in the patient with pyorrhea or other gum disease.

Bronchoscopic aspiration, removal of foreign body, dilatation of stricture aided materially. It was not until antibiotics particularly penicillin became available that real progress was made. Penicillin in large doses worked wonders and cured a large percentage of abscesses.

Abscesses which have not responded to rest, postural drainage, and bronchoscopic drainage should be surgically drained in one or two stages, depending on obliteration of the pleural cavity locally without waiting for the process to become chronic. If drained adequately early with removal of the dead tissue the surrounding lung tissue expands rapidly to obliterate the cavity. In the chronic stage the sclerotic wall is rigid and will not close leaving a chronic cavity with a bronchial fistula. With the advent of chemotherapy, particularly with penicillin, many acute abscesses clear rapidly, often completely. Less than 10% require drainage and the number of complications is reduced. Drainage in the chronic stage for control of hemorrhage might result in

months of dressings and plastic procedures.

With improvement in resection technique and intensive chemotherapy chronic abscesses may be resected instead of drained with low risk and short hospital stay. Our service at the Minneapolis General Hospital[278] from the mid-thirties produced a considerable number of abscesses successfully treated in standard manner by early drainage in one or two stages. If improvement was not rapid and progression occurred, resection was undertaken from mid-1938. With adequate antibiotic therapy few resections became necessary.

Bronchoscopy and Esophagoscopy

Bronchoscopy and esophagoscopy have played an increasingly important role in the diagnosis and treatment of intrathoracic disease. Bozzini[39] in 1807 examined the upper end of the esophagus. Horace Green[305] of New York in 1828 demonstrated an ulcer of the larynx with instruments. Voltolini[413] and Waldenburg[415] in 1860 devised an esophageal speculum. Waldenburg in 1868[415] devised an esophagoscope 8 cm. long using a mirror and inspected a pharyngeal diverticulum. Kussmaul[223] in 1868 did the first direct esophagoscopy using a 43 cm. Desormeaux urethrascope and saw a carcinoma of the esophagus. Von Hacker was the first to stress the value of direct vision. A. Kussmaul,[223] who apparently was the first to wash out the stomach in gastric dilatation, is reported to have attempted to look down the esophagus and stomach unsuccessfully in 1869. Trouve devised a polyscope using prisms and lenses in 1873. Mikulicz in 1881 used a tube with optical apparatus and later with larger tubes examined the stomach. A new instrument was devised by Storerk in 1881. Joseph O'Dwyer[305] developed his intubation tubes for laryngeal diphtheria in 1885. Killian in 1897 removed a bone by tracheotomy and tracheoscopy and did a bronchoscopy in 1898. Killian[305] in 1902 stated that direct esophagoscopy was the only reliable way of removing foreign bodies. Einhorn devised an esophagoscope with an auxiliary tube for the light, in 1902. Jackson in 1904 combined the tube of Killian with the light tube of Einhorn.

Foreign bodies likewise directed interest in this field in Minnesota. Dr. C. H. Mayo[263] in 1895 removed a lost O'Dwyer intubation tube through a tracheostomy. Again in 1896 he[263] reported removing a citron seed and a kernel of corn through a tracheostomy and three from the esophagus, a chicken bone through an esophageal incision, a prune stone from the lower esophagus and an oyster shell pushed into the stomach for removal. The next year, 1897, through a cervical esophagotomy incision[264] he removed a vest buckle which had been demonstrated by an Xray taken by Dr. J. Grosvenor Cross.

Dr. George Eitel[96] assisted by Dr. Dunsmoor in 1898, successfully removed a partial dental plate impacted in the esophagus for six years through a left esophagostomy incision.

Dr. Arnold Schwyzer[365] of St. Paul in 1903, using a Killian scope with a Casper panelectroscope brought from Europe, removed a foreign body through a tracheostomy wound for the first bronchoscopy in the Twin Cities. Primarily a general surgeon with wide interests, he possessed a keen mind and wide knowledge and added much in many fields to many meetings. In this field he did many foreign body extractions from the trachea and esophagus, using radium in the treatment of carcinoma, and drained mediastinal abscess. He also did the first cystoscopy in Minnesota in 1894.

Drs. Plondke and Schwyzer[365] of St. Paul in 1904 did a tracheostomy for foreign body, the patient coughing out the kernel of corn when the trachea was opened. Dr. William Lerche[242] came to St. Paul in 1905 from Austria where he was trained and for years was a leader in this type of work. He removed a tack from the bronchus in 1908, the first peroral procedure of this type in St. Paul, and listed 40 such procedures with mortality. He made many contributions over the years, including esophageal sounds, a loop for closing open safety pins, and improved esophagoscope, a calibrated Kohlman dilator for strictures, and later surgery for mediastinal abscess. Following him in St. Paul was Dr. D. Greth Gardner[123] who became his associate in 1920. Also in 1920 Dr. Charles Connor[62] came to St. Paul after training with Chevalier Jackson, working at Miller, Children's and the University Hospitals. Dr. John J. Hochfelzer, Austria-born and Vienna-trained, entered practice in St. Paul in 1924 followed in 1930 by Dr. Jerome Hilger.[172] in 1932 by Dr. N. Logan Leven[239] and in 1946 by Dr. Coleman Connolly.

Dr. Frank Todd[395] in Minneapolis reported removing a peanut in 1909 and a tack from the

right upper bronchus using a Jackson scope in 1904. Dr. J. D. Lewis did occasional foreign body cases at the Minneapolis General Hospital. Rizer[331] who had done bronchoscopy and esophagoscopy for Sippy of Chicago came to Minneapolis in 1915 where he continued to do these procedures in his own practice and at the University. He also used the string guide in esophageal dilatation. Kenneth Phelps[311] came to Minneapolis from Johns Hopkins in 1919 and from that time on was the dean of the profession in the city, doing most of that work in private practice and at the University and Minneapolis General Hospitals. Horace Newhart[311] and his associate, Walter Camp, performed these procedures using the Killian instruments in 1920. Virgil Schwartz[364] after finishing his residency in Otolaryngology at the University and General Hospital spent a year in Vienna with Hasslinger, returning to the City to private practice in 1923 and the service at the General, using the Hasslinger instruments and later the Jackson type. All of the previous men were nose and throat specialists. Arthur Kerkhof[201] an internist upon completion of his residency at the General Hospital in 1932, was sent by Dr. George Fahr to Vienna for a year of study with Hasslinger, returning to private practice as an internist doing endoscopic work as well.

Lawrence R. Boies[36] began practice in Minneapolis in 1931 in Otolaryngology and Bronchoscopy, continuing for a number of years until he became head of the department at the University. J. Bain Carey,[46] an internist, interested in gastroenterology, after a period of training with Schindler returned to do gastroscopy with the Schindler flexible gastroscope in private practice and at the University Hospital. Soon, as the demand for diagnostic endoscopy increased as chest conditions were more carefully studied, a number of well-trained and grounded endoscopists appeared: Priest, Holmberg, Richardson, Smith, Glaser and others.

With the interest previously shown by the surgeons at the Mayo Clinic, it is not surprising that the medical side also became involved. Henry S. Plummer[312,315] came to Rochester in 1901 and immediately became interested in the esophagus and its troubles and continued this interest until 1923 when he turned the work over to Porter P. Vinson.[312] His contributions included treatment of stricture by dilators and the Albee string saw, dilatation over a string guide (originated by Mixter), retrograde dilatation, an improvement of the Russell[345] hydrostatic dilator, removal of foreign bodies, recognition of carcinoma and biopsy of tumor. He described the Plummer-Vinson syndrome[315] in a paper in 1914 written and presented, but not published. He was a mechanical genius and in his own shop made many of his own instruments for special problems. He is known to have traveled to St. Paul to observe Dr. Lerche at work. Eccentric in many ways but a true genius along many lines, he was responsible for a great number of mechanical improvements about the Mayo Clinic and its buildings.

Porter P. Vinson[312] came to the Clinic in 1917 joining Plummer and later taking over the endoscopic work as well as internal medicine. He was joined by Herman Moersch[312] in 1924 and later by Arthur Olsen, Herbert Schmidt, and others. From the beginning endoscopy at the Clinic has always been in the medical chest department.

The first endoscopist in Duluth was N. H. Gillespie[91] who brought endoscopes from Vienna in 1908. Later beginning in 1910 Tildcrquist[91] began this work and continued for years, being joined in 1926 by Anderson Hilding[91] who continues to date. Paul Boman from the Duluth Clinic began this work in 1922. Keith Fawcett of the Duluth Clinic introduced the work to the Nopeming Sanatorium in 1937 where it was taken over in 1939 by Robert Davies and in 1946 by Reno Backus. Herbert Carlson[49] at the Minnesota State Sanatorium at Ah-Gwah-Ching did bronchoscopies from 1937-39. C. L. Oppegaard[68] began in 1940 at Crookston.

C. L. Chambers[284] of Bismarck, North Dakota, was doing bronchoscopies in 1924 and C. O. Robinson, esophagoscopies in 1926. McCannel,[284] a nose and throat man, and Paul Breslich[284] an internist, pioneered endoscopy in Minot. Nelson Youngs[435] of Grand Forks has been active in this field since 1934. George A. Dodds,[85] 1937-39, and later George Loeb[250] did endoscopic work at the State Sanatorium at San Haven.

John Gregg, Sr.[65] of Sioux Falls, South Dakota, reported removing a kernel of corn from the bronchus in 1922, the first in the state. Paul Bunker[44] of Aberdeen removed a foreign body in 1930, the second in the state. He received

the Chevalier Jackson award of the American Bronchoesophageal Association in April, 1966, the sixth individual to be so honored.

Tuberculosis

Tuberculosis has posed a threat to the human race since the beginning of recorded history. It is properly called "Captain of the Men of Death." Almost every type of treatment has been tried in this disease including the "Royal Touch" for scrofula. William of Orange, disbelieving in its value but for political reasons continuing it, added the following: "and God give you better health and better sense."

Tuberculosis in Minnesota and the Dakotas

The early explorers and settlers of Minnesota came from Europe where Tuberculosis was a common disease. The Indians were apparently free of this until contaminated by the white man. Williamson,[425] a missionary physician at Lac qui Parle in western Minnesota from 1835 to 1846, stated that half of the Indians over the age of ten who died of disease had tuberculosis. More settlers arrived in the fifties and brought disease with them. Commercial interests[279] to encourage more settlers advertised that the "elixir in the air" of Minnesota cured consumption, bronchitis and other diseases of the chest. Health seekers, ever in the hope of a magic cure, came in large numbers, some to recover, others to succumb, and to spread their disease to others. Among the famous health seekers to visit Minnesota was Henry David Thoreau[394] from Massachusetts who in 1861 took a trip up the Minnesota river to Redwood Falls. Another famous health seeker was Dr. Edward Livingston Trudeau,[394] one of the pioneers in the treatment of tuberculosis. He arrived in St. Paul in the fall of 1873 febrile, but he walked about and went duck shooting. He spent the winter here, returning to New York in May of 1874.

The State Legislature of 1903 authorized the construction[284] of a State Sanatorium near Walker on Leech Lake which was opened in 1907. The private sanatorium of H. L. Taylor was opened in 1903 at Pokegama in Pine County and the same year a tuberculosis unit was started at Luther Hospital, St. Paul. Later it was transferred to Ancker Hospital. The sanatorium law of 1913 provided for construction of 14 county and district sanatoria for the treatment of tuberculosis. In line with the medical thinking of the day, all of these were placed in isolated locations or well away from other established medical or surgical facilities with the exception of the Pavilion at Ancker Hospital. This proved to be a very serious handicap when surgery came into the treatment picture and a great inconvenience to the visiting and consultating staff. Surgical facilities were eventually provided at Glen Lake, Nopeming, Mineral Springs, Sunny Rest, and the State Sanatoriums, but operated under many handicaps. The Pavilion at Ancker Hospital was of course part of a general hospital.

The state of Minnesota from 1915 to 1925 was averaging at least 4,000 cases of Tuberculosis per year on an increasing scale. There was a dire need for facilities for isolation and treatment to meet this challenge. The institutions built under the sanatorium law are here listed with maximum[284] capacity.

		Beds[284]	
1905	Pokegama, Pine City, Private Closed 1944	42	
1907	Thomas Hospital, Minneapolis Closed 1930	20	
1907	Hopewell Cottage, Minneapolis Closed 1924	130	
1907	Minnesota State Sanatorium, Walker Closed 1962	240 115	Whites Indians
1912	Nopeming, St. Louis County near Duluth	300	
1913	Otter Tail, Battle Lake	48	
1914	Ancker Hospital, St. Paul	188	
1915	Mineral Springs, Cannon Falls	100	
1916	Sunny Rest, Crookston	60	
	Lake Julia, Puposky	52	
	Glen Lake, Hennepin County, Minneapolis	680	
	Sand Beach, Lake Park	42	
1917	Buena Vista, Wabasha	30	
	Southwestern Minnesota, Worthington	45	
	Riverside, Granite Falls	48	
1918	Oakland Park, Thief River Falls	65	
	Fair Oaks Lodge, Wadena	36	

As of July, 1968, all of these have been closed except Glen Lake which is now the State Sanatorium but has under fifty Tuberculous patients, Ramsey County Hospital (Ancker), Nopeming now with a much reduced capacity, and Mineral Springs.

The early sanatoria had little to offer in the way of treatment except prolonged bed rest which might even be continued for years. Under such a program a patient with minimal tuberculosis had at least a 90% chance of recovery, one with moderately advanced disease about 60% chance, while

the far advanced case only 10%, unless some other help could be added. The first procedure available was artificial pneumothorax. It was primarily a bedside type of treatment with no patient too old or too young or too ill.

Pneumothorax

The Hippocratic school[216] is reported to have injected air into the pleural cavity to facilitate drainage in empyema patients. James Carson[52] in 1822 following numerous experiments on a variety of animals reported that one lung could be safely collapsed by injection of air into the pleural cavity and suggested that it be used in treatment of tuberculosis. Daniel McRuer[269] of Bangor, Maine, in 1835 made the suggestion that puncture of the chest to admit air to suspend the function of the lung might be of value in phthisis. Potain[318] in France in 1880 suggested aspirating a pleural effusion in tuberculosis and replacing with air, and in 1884 carried out this operation. Carlo Forlanini[109] from the University of Pavia in Italy in 1888 carried out the same procedure and in 1892 established the first primary therapeutic pneumothorax. R. W. Parker of London, discussing a paper "Hemoptysis treated by artificial pneumothorax" by W. Cayley, quoted him as recommending "the injection of filtered and carbolized air into the pleura such as he had advised in the treatment of certain kinds of empyema." John B. Murphy,[283] of Chicago in 1895, apparently in ignorance of Forlanini's previous work, established pneumothorax for the treatment of pulmonary tuberculosis and in his presidential address to the American Medical Association in Denver in 1898 reported upon its use and other procedures for tuberculosis. Alarmed at the enthusiastic reception which this procedure received and fearing that he would become known as a medical man rather than as a surgeon, he turned the treatment over to his associate, Dr. August F. Lemke.[235] He followed up the treatment aggressively and by 1901 had treated 350 cases whereas Forlanini by 1911 had only 86. He also must be credited with performing the first alternating bilateral pneumothorax. The death of Lemke certainly delayed the spread of pneumothorax treatment in this country for several years while European physicians continued to develop it.

A publication of Adams in 1887 cited a case of pulmonary hemorrhage which was controlled by the occurrence of a spontaneous pneumothorax. Walker Schell[358] of Indiana in 1898 reported injecting 1,400 cc of nitrogen into a pleural cavity to stop pulmonary hemorrhage in tuberculosis. H. P. Loomis[252] in 1900 reported 18 cases of which eight were started to arrest hemorrhage.

Xray in 1895 added much to the knowledge of lung disease and control of pneumothorax treatment. Christian Saugman[349] of Denmark added the water manometer to the pneumothorax machine in 1907, greatly increasing the safety of the procedure.

When Lemke died, interest in the treatment in this country decreased for a number of years and few published articles appeared in the American literature. About 1912 following the appearance of several articles by Mary Lapham[231] of North Carolina, and Pratt, Robinson, Floyd and Balboni[16] of Boston describing their experiences, Samuel Robinson[335] and Cleveland Floyd developed a compact pneumothorax apparatus with a water manometer which became the model for use throughout the country. Nitrogen was used for injection in controlled amounts with controlled pressure. In 1912, Cleveland Floyd[284] of Boston established the orginal pneumothorax on Edward L. Trudeau, reducing his fever and rendering his sputum negative. Gerald B. Webb[424] of Colorado Springs brought pneumothorax to the Rocky Mountain region in 1912 and subsequently with his associates, by analysis of the residual gas in the pleural cavity, demonstrated that the composition was approximately the same whether nitrogen or air was originally injected. This work resulted in the use of filtered air and the abandonment of nitrogen. By the twenties pneumothorax was in use in most of the larger sanatoria of the country, as the first surgical procedure to use in the patient who did not improve under bedrest or who developed serious bleeding.

H. Longstreet Taylor[393] of St. Paul in 1899 performed the first active procedure directed against pulmonary tuberculosis in the state by establishing the first artificial pneumothorax. He injected two quarts of nitrogen into the pleural cavity of a young girl at Bethesda Hospital. The patient improved for a month or so and then the symptoms returned. Unfortunately the treatment was not repeated. He likewise did the first pneumothorax at Pokegama in 1921.

The first therapeutic pneumothorax was established at Glen Lake Sanatorium in 1916,[131] more

than four years before the first x-ray equipment was installed. It was given probably by Dr. Fred W. Wittich[131] who was consultant to the Glen Lake Sanatorium at that time. Dr. Wittich had in 1914 with C. H. Vrooman[414] of the Provincial Sanatorium at Kamloops, British Columbia, Canada, published a paper "Apparatus for Producing Artificial Pneumothorax."

Dan Wheeler[292] of Nopeming Sanatorium near Duluth established the first pneumothorax at the Head of the Lakes in 1924. We have no records of such treatment at Ah-Gwah-Ching, the State Sanatorium before 1937.

To Lemke must go the credit for performing the first alternate bilateral pneumothorax. Fagiuoli and Ascoli[103] in 1912 induced the first simultaneous bilateral collapse and continued it, but it did not become a popular treatment. Everett K. Geer[125] of St. Paul is credited with the first simultaneous collapse in the state of Minnesota in 1922 publishing a report in *Minnesota Medicine* in 1923. Glen Lake's first bilateral collapse was started by Dr. Harold Boquist[131] in 1924. An accidental pneumothorax occurred at the time the second side was established, but no dyspnoea occurred as there was considerable reserve breathing space on the opposite side at the time. The patient is in good condition and symptom-free to this date, 44 years later. Dr. P. M. Mattill[203] and I reported on 108 patients so treated by the staff of Glen Lake Sanatorium in 1927. Alexander Josewicz[234] must be credited with the first diagnostic pneumothorax territory which was in Minneapolis.

The value of pneumothorax treatment has been amply demonstrated by the extent of its use (up to 50% of patients) in some large institutions and the thousands of patients who recovered from tuberculosis because of it. No patient was too old or too young or too ill to be tried on this bedside procedure. That there were disadvantages and complications must be admitted, but many of them were avoided by careful management. The worst form of mishandling was the indefinite continuation of unsatisfactory collapse and trying to "stretch" limiting adhesions.

At one time ambulatory pneumothorax enjoyed a brief period of popularity. It was used by force of circumstances in Chicago where a huge load of active cases of Tuberculosis accumulated with all available hospital beds occupied. The health authorities hoped that by pneumothorax collapse, some cavities might be closed and sputum rendered negative, thus reducing the danger of dissemination of the disease about the City. Jay A. Myers was the only physician in the local area to use it to any extent.

An illustration of the extent of the prevalence of pneumothorax among discharged patients comes from my own office. When in World War II, I was making arrangements to transfer my patients to other physicians as I prepared to enter service, my secretary found that we had 118 working patients with pneumothorax, with 18 of them bilateral.

Intrapleural Pneumonolysis

The success of the pneumothorax treatment of tuberculosis was dependent upon finding sufficient free pleural space to permit collapse of the involved areas and closure of the cavity. Limiting adhesions frequently defeated all efforts to control the disease. Hans C. Jacobaeus[182,183] of Stockholm, Sweden, in an attempt to remedy the situation conceived the idea of sectioning the limiting adhesions and devised an endoscope for visualizing them in 1913 and subsequently severed some with galvanocautery. Jacobson in 1914 and also Heuve[171] cut some under fluoroscopic guidance. Jacobaeus visited the United States in 1921, giving lectures in various cities including Minneapolis, and on November 14, 1921, delivered one[287] which I attended at the Mayo Clinic. Glen Lake Sanatorium purchased the proper instruments soon after that, permitting Frank Jennings[131] to undertake the procedure first in 1923. He was able to cut a few small strings but was unable to close the cavity held open by a large thick adhesion totally unsuitable for section. Gradually under continued pneumothorax this cavity closed, the patient obtaining a good result which has persisted to date. The instruments then remained unused on the operating room instrument shelves, as many very expensive special instruments do, until July 14, 1927 when I explored a patient's chest but was unable to sever all adhesions. Her cavity was later closed following an open thoracotomy with manual compression of the cavity-bearing adhesion without severing it. I continued to do this type of surgery at Glen Lake over the years and introduced it to Mineral Springs Sanatorium, Wabasha, Sunny Rest in Crookston, Pokegama, Nopeming and Walker in the late thirties. Herb Carlson[49] had

previously done several cases there between 1937-39.

Complications were: subcutaneous emphysema, occasionally with loss of collapse, bleeding from the parietal stump of the severed adhesion, pleural effusion or empyema, usually tuberculous. Empyema was the most frequent, possibly reaching 10%, depending upon how drastic the surgeon became in attempting to extend the indications.

The results from adhesion cutting depended upon successful section of most, not all, adhesions holding the cavity open; in other words, converting an unsatisfactory pneumothorax into a satisfactory one, if no complications ensued. With the advent of specific drugs the use of pneumothorax dropped rapidly and likewise the need for pneumonolysis.

Extrapleural Pneumonolysis and Pneumothorax

The use of extrapleural stripping came early into the field of thoracic surgery. Block[33] in 1883 performed a bilateral extrapleural resection of apical disease upon his cousin. When the patient died soon after the operation and the disease proved to be non-tuberculous, he took his own life. Tuffier[397] of Paris in 1891 successfully performed an apical stripping and then resected a tuberculous nodule from the lung. The marvel is not that he was able to do it, but how he was able to diagnose the lesion in the first place for Rontgen did not discover Xray until four years later. Schlange[360] in 1907 resected six centimeters of the anterior third rib, did an extrapleural pneumonolysis to control pulmonary hemorrhage and packed the space created with iodoform gauze. Tuffier[398] in 1910 did an extrapleural stripping and filled the space with a free fat graft. Later in 1913, Baer[13] used paraffin; Wilms, bone fragments; and Guilder and Kroh[219] and later Harvey, an inflated rubber bag. Shivers[370] of Colorado Springs and Archibald of Montreal used the pectoral muscles. Tuffier[398] before using the "fat pack" had once filled the space with air as an extrapleural pneumothorax, while Jennings[184] had done the same, leaving an external fistula to the skin. Bull, Shivers,[371] Schreiber[363] and Stocklin used apicolysis in association with thoracoplasty. Wilms[427] and Sauerbruch[353,354] also used pneumonolysis with thoracoplasty. Jessen[187] and Unverricht[402] did an extrapleural stripping over the attachment of a large adhesion in pneumothorax.

To my knowledge no one in this area performed extrapleural pneumonolysis until at Glen Lake we carried out the first "paraffin pack"[131] in 1934. This pack is still in place and has caused no trouble. Over the years we carried out more than 58 such operations, six of them bilateral, with no complications for five years in patients with obliterated pleural space. We then began to see complications such as persistent effusion about the paraffin, migration of the wax, perforation of the lung with expectoration of paraffin strings and infection of the space, confirming Ralph Matson's[261] statement that "they worked very well for five years, then blew up." Now although many of these patients survived, only about a half-dozen still carry their packs, the others having been removed because of complications.

In 1938 instead of using paraffin in the extrapleural space, we began to use pneumothorax to maintain the collapse and continued refills as in ordinary pneumothorax. G. A. Hedberg[292] who had been working with us for some time, did his first extrapleural pneumothorax in 1939 at Nopeming Sanatorium. The use of air filling for the extrapleural space eliminated many of the complications of this procedure. This type of collapse gave some chance of discontinuation later. The presence of some free pleural space did not contraindicate its use as it did in true extrapleural procedures, but permitted the extrapleural stripping of a large limiting adhesion and the conversion of a previously unsatisfactory pneumothorax to a satisfactory one. Many of these were filled with mineral oil and continued as an extrapleural oleothorax. The results were quite satisfactory. This procedure offered a relatively safe means of bilateral collapse without great reduction in vital capacity.

Phrenic Nerve Surgery

Surgery upon the phrenic nerve was first suggested by Steurtz[386] in 1911 for treatment of a left lower lobe bronchiectasis. Harrington, in discussion of a presentation on phrenic nerve surgery by Howard K. Gray[142] before the Mayo Clinic staff, stated Bardenheuer[18] did the first such operation in 1912. Sauerbruch[355] in 1913 performed phrenic interruption and reported five cases with good results. Gradually use of the technique spread, at first by evulsion of the trunk (phrenic

exercsis) from a cervical incision, later by cutting the main trunk, later with interruption of accessory branches which occur in about 30% of patients, both of these giving a permanent paralysis of the diaphragm. Subsequently the main trunk and branches were crushed (phrenemphraxis) to give a temporary paralysis which lasted about six months, though some were permanent depending upon the length and the severity of the crush. The physicians in this area never became this enthusiastic about it, realizing the importance of the diaphragm in patients with bilateral disease where the loss of its motion might preclude the later use of other necessary surgery because of reduced respiratory reserve induced by it. The first such operation at Glen Lake was done by A. A. Law[131] in 1924. Only seven such operations were done to 1927 though more were done subsequently, most of the temporary variety, after I took over the surgery at the Sanatorium. Later I started this type of collapse at Mineral Springs and Sunny Rest. Carlson did a[49] number of phrenic operations at the State Sanatorium during his term there, 1937-39. Chapman[53] and Gillespie carried out the operation at Nopeming. Law also did some at the University Hospital. The surgeons at the Mayo Clinic used the procedure not only for tuberculosis but also for bronchiectasis and with other surgery in diaphragmatic hernia. Later it became an aid in space obliteration following lobectomy and pneumonectomy.

Ligation of Pulmonary Artery

Kuttner[224] in 1878 was the first to follow the changes in dogs after ligation of the pulmonary artery. O. Bruns and Sauerbruch[43] in 1911 repeated the experiments and at the end of three months noted marked fibrosis of the lungs. K. Kawamura[196,197] in 1913 again repeated the experiments on rabbits and dogs with similar results. Willy Meyer in 1913 tried it in bronchiectasis clinically with partial success. Sauerbruch[352] used it in 14 cases of bronchiectasis with some success and noted extensive fibrosis and retraction.

Karl Schlaepfer[361] of Baltimore in 1923-24 repeated the studies and noted intense fibrosis and retraction in shorter time than the pneumothorax or thoracoplasty. He mentions obstruction of the bronchus by fascia as suggested by Halstad and Crowe. A few cases were done by Sauerbruch, Kuttner and Willy Meyer. There are few other reports of its use except occasionally to control hemorrhage. I know of no local use of this procedure.

Dr. H. Morriston Davies[76] in 1913 ligated the pulmonary artery in an attempt to control pulmonary tuberculosis.

Scalenectomy and Intercostal Neurectomy

Scalenectomy

Sections of the insertions of the scalene muscles in the neck were studied experimentally by Kochs, Els[215] and Junkersdorf in 1930 on monkeys and they proposed its use to relax the upward support of these muscles on the first and second rib. Gale and Middleton[121] independently made the same suggestion. John Alexander[5] of Ann Arbor carried out a few operations but the effect on clinical tuberculosis cases was not striking so it was soon forgotten. The procedure is automatically carried out when the first and second ribs are resected in thoracoplasty.

Intercostal Neurectomy

Warstat[423] of Konigsberg experimentally avulsed the intercostal nerves in rabbits and dogs and interrupted the phrenic nerve. Respiratory function ceased on the side as the chest wall fell into cadaveric position. Studies subsequent to intravenous injection of tubercle bacilli showed a few noncaseous tubercules on the operated side but many and larger lesions opposite. Later two patients were operated upon and improvement noted.

Schepelmann[359] experimenting on rabbits found that considerable immobilization of the side occurred but did not recommend it for humans. Hug[177] using dogs noted the same effects. Friederick[114] in 1913 carried out the operation on a human but was dissatisfied with the result obtained. Alexander in 1920 carried out the procedure on animals in conjunction with phrenic nerve interruption and was impressed by the amount of immobilization and flattening of the chest wall. Leota and Cimino[237] produced the same effects by injecting the intercostal nerves with alcohol. Alexander[5] first used the procedure on patients in 1927 and with Strieder[388] reported its use in 20 patients unsuitable for thoracoplasty because of very active disease and felt there was distinct benefit. It was never adopted very enthusiastically and was soon forgotten. I find only five records of its use as an independent procedure in the Glen Lake operative records.

Thoracoplasty

The term "thoracoplasty" means a plastic opera-

tion on the chest wall and may include anything from removal of a rib or two to drain an empyema to the most radical Schede operation with removal of extensive portions of the thoracic wall including rib, intercostal muscles and parietal pleura. As used for many years in the treatment of chronic empyema to obliterate pleural space, the lung was fixed and bound down, the pleural layers thickened and the mediastinum stabilized leaving the lung with very little function. Such operations as the Estlaender,[102] Wagner-Quenu and Schede[357] were used and fairly well tolerated.

The problem in tuberculosis was much different. The lung itself was diseased, the pleural layers though fused were not greatly thickened, the mediastinum was not fixed or stabilized. The extensive rib resections of the early days resulted in chest wall and mediastinal flutter with a mortality of at least 30%.

Thoracoplasty, for years the last resort in the treatment of pulmonary tuberculosis, developed from surgical attempts to obliterate the pleural pockets in chronic empyema. De Cerenville[78] in 1885 is credited with first using it in the treatment of tuberculosis, reporting four cases done for apical disease, resecting three and a half centimeters of ribs—two and three anteriorly, and in two draining cavities. Quincke[332] in 1888 carried out similar operations. Carl Spengler[380] in 1890 through a periscapular incision resected larger segments in patients with pleural effusion and used the term "extrapleural thoracoplasty." Boiffin[37] in 1894 resected segments of ribs at their angles in treating empyema. Julien Gourdet [136] in a thesis published in 1895 reported the results of his studies in which he found that the best collapse was obtained from resections at the angles of the ribs. Turban[399,400] in 1896 resected rib four to six and six months later seven to nine for tuberculosis. Garre and Quincke[322] in 1901-03 carried out thoracoplasty, supplementing it with extrapleural pneumonolysis. Bier[26] and Landerer also did thoracoplasty at this time. Friederick in 1907, at the instigation of Brauer who recognized the need for more collapse, resected larger segments (10-25 cm.) of ribs two to nine in one stage. The patient survived and was improved some 14 months later. The operation was done through a U-shaped (Schede) type of incision under light, local anesthesia and in a very rapid manner. There was terrific shock. Chest wall and mediastinal flutter followed. Brauer later reported that three of seven died and Friederick had four of eight fatalities. Friederick[16] later removed the first rib also. By 1911 there was a report of eight deaths in 29 cases (29.6%).

Sauerbruch[352] in 1909 carried out his paravertebral thoracoplasty and by 1911 had divided the surgery into two stages. Wilms[426] in 1911 demonstrated the value of the experimental work of Gourdet,[136] Eden[334] and Robinson with columnar resection. Later he used a parasternal incision to resect more rib. Brauer and Spengler[41] in 1913 carried out their subscapular paravertebral thoracoplasty. Brauer later worked out an anterior incision following Becker's suggestion.

Edward Archibald[12] of Montreal has for years been credited with carrying out the first thoracoplasty on this continent in 1917. This is probably true if one considers a thoracoplasty of the Wilms-Sauerbruch type. However, Leonard Freeman[113] of Denver, Colorado, in 1909 reported two patients upon whom he had operated in 1901 and 1902, resecting segments of ribs two and three anteriorly and then applying strong compression over the resected area with a truss-like arrangement to produce a marked depression. One patient, a 19-year-old boy from Denver National Jewish Hospital had a hemorrhagic phthisis with quite a large cavity below the left clavicle. He had had a spontaneous pneumothorax and empyema some months before and had had an extensive Estlander operation done without affecting the cavity, although two-thirds of the lung was compressed. He was raising several ounces of sputum, was emaciated and not improving. Five months after the operation he was improved and the sputum almost gone. Eight years later it had not returned.

The second patient treated in similar manner with resection of three-inch segments of the second and third ribs anteriorly and truss compression likewise obtained a good result with cavity closure and no recurrence seven years later. The remarkable thing about this result with very localized anterior compression lies in the fact that most tuberculous cavities lie in the apical posterior segments of the upper lobe rather than anteriorly. The operation which Dr. Freeman did was the same as DeCerenville's[78] thoracoplasty of 1885 with compression added. Later in May of 1920, Freeman performed[113] two thoracoplasties of a modified Sauerbruch type, ribs one to nine

in one stage.

Shortle and Geckler[371] in 1922 reported four cases of thoracoplasty done in 1920 although neither of the authors was a surgeon. Shortle had been an assistant to Karl Spengler during the winter of 1907-8. Geckler had been an assistant to Ludolph Brauer at Marburg when he suggested to Friederick the operation later modified by Sauerbruch. The first two cases in May, 1920, were done by Leonard Freeman[113] of Denver in Albuquerque for Shortle and both survived. The other two were done by Cornish and both died. I well remember at Glockner Hospital in Colorado Springs in 1924-5 watching Freeman doing a thoracoplasty on one of our patients from Cragmoor Sanatorium and treating the patient for deep shock which developed when at the conclusion of an upper stage thoracoplasty he very forcibly manually compressed the deribbed chest wall. John Alexander's[3] book "Surgery of Pulmonary Tuberculosis" published in 1925 while he was on the flat of his back in bed with multiple tuberculous lesions and before he had ever done a thoracoplasty became the standard text and reference book on treatment of tuberculosis. Up to 1918 less than 100 thoracoplasties were recorded.

Carl Hedblom[284] of the Mayo Clinic is credited with doing the first thoracoplasty for tuberculosis in Minnesota and the surrounding territory in 1919. E. P. Quain [321] of Bismarck, North Dakota, in 1920 did a multiple rib resection (six ribs) on a seven year old girl. This was for chronic empyema and not for tuberculosis. Arthur A. Law did the first such operation in the Twin Cities at Glen Lake Sanatorium[131] on January 22, 1922 on a 64-year-old man who survived for over 14 years.

Law was a superb surgeon, a fascinating teacher, interested in everything new and like many of the surgeons of his day a speedy operator. Speed was then considered a very important factor in early surgery for tuberculosis and in this field there was no one better fitted than Dr. Law. I have assisted him in an upper stage thoracoplasty, five ribs—complete from incision to the last stitch of closure in eleven minutes and lower stage six ribs in nine minutes. Shock was a constant aftermath and blood loss not a small factor. Later after we had taken over and chose to do the surgery under local anesthesia time was less important, taking an hour or hour and a half if necessary. Shock was rare, blood loss reduced, and a cleaner and better operation performed. Over a period of time our average blood loss at surgery plus the first two days drainage on the dressings was: upper posterior stage five ribs, 450 cc.; intermediate posterior, 290 cc.; lower posterior, 195 cc.; and anterolateral four ribs, 250 cc. Law continued this work until 1927 when he resigned because of ill health, turning the surgery over to this author who carried on to 1940 when Victor K. Funk[120] and Leonard M. Larson took over.

Stanley R. Maxeiner[262] of Minneapolis did his first thoracoplasty in May, 1924, at Parkview Sanatorium in that city. All of the old records before 1933 for Ancker Hospital, St. Paul, and all records from Pokegama Sanatorium at Pine City have been destroyed so we are a little uncertain as to exact dates from these two institutions. As near as can be ascertained L. E. Daugherty[75] of St. Paul performed his first thoracoplasty for tuberculosis in 1924 at Ancker Hospital and at Pokegama in 1925. Unconfirmed rumor has it that in the early days, Arthur Colvin[61] did a couple of extensive one stage thoracoplasties with fatal results convincing him it was a bad operation. Daugherty was followed by D. Greth Gardner who carried on in chest surgery as well as bronchoscopy for many years until Coleman Connolly, Logan Leven, Lyle Tongen, Gernard G. Lannin, and Sam Hunter entered the field.

T. O. Young and Dan Wheeler[434] carried out the first thoracoplasty at the Head of the Lakes at St. Luke's Hospital in 1925. In 1926 T. L. Chapman[53] and M. G. Gillespie did thoracoplasties for Nopeming at St. Mary's Hospital, Duluth. G. A. Hedberg of Nopeming reports doing thoracoplasty on 20 patients at St. Mary's in Duluth in 1937-38, and the first at Nopeming Sanatorium[292] in 1938, upon completion of operating facilities at that Institution. Law did a number of such cases in the early days at the University of Minnesota Hospital followed by Wangensteen, Varco and Herbert Carlson and others of the staff. While on the staff of the Minnesota State Sanatorium at Ah-Gwah-Ching, Carlson[49] carried out 37 stages of thoracoplasty, 1937-39. The first such operation at Crookston, Minnesota, was done by this author at Bethesda Hospital in Crookston for Sunny Rest Sanatorium in 1929. A few others followed until late in 1930 when M. O. Oppegaard[297] assumed the surgery.

Thoracoplasty in North Dakota was initiated in 1920 by A. P. Quain[321] of Bismarck for a nontuberculous chronic empyema on a seven-year-old girl. The early patients with tuberculosis from the State Sanatorium at San Haven near Dunseith were sent to the Mayo Clinic. Angus Cameron, Sr., of Minot[85] in 1935 operated upon two patients. When G. Alfred Dodds[85] took over as superintendent in 1937 he also took over the surgery for the Institution. He had been trained in tuberculosis at Glen Lake Sanatorium and soon instituted an intensive collapse therapy program with up to 71% of the patients under some such treatment. He did over 52,000 pneumothorax refills and did over 420 thoracoplasty stages under local anesthesia with 0.75% mortality. Later in private practice at first in Valley City and then with the Fargo Clinic, Dodds continued to do chest surgery and became the first in North Dakota to be certified by the Board of Thoracic Surgery. Later Fritzell of Grand Forks Clinic, Grant Tolsted of Bismarck and Angus Cameron, Jr., of Minot came into the field.

Cedric Northrup succeeded Dodds in 1939 and was soon joined by William Walbank[416] who was surgically trained and took over the surgical program until 1950. George Loeb[250] joined the staff in 1944 working with Walbank until he left for Toledo in 1950. The surgical program from 1944 to 1958 was very active. The first pulmonary resection for tuberculosis from the Sanatorium was sent down to St. Mary's[351] to us for a pneumonectomy in the fall of 1947. The patient was a Public Health nurse, who is well today. Subsequently with the introduction of adequate antituberculosis chemotherapy, all the major resections up to 1964 were referred to St. Mary's Hospital, Minneapolis.

South Dakota with its smaller population and no large cities naturally presented few opportunities for special work. Very little chest surgery was done until the last 10 years. Godfrey Cottam[65] of Sioux Falls did the first thoracoplasty in 1933 on a patient from the State Sanatorium at Custer. This arrangement continued for a time when fear of tuberculosis in a general hospital ended the transfers from Custer and the State Indian Sanatorium. The patients then for several years were sent to this author at St. Mary's Hospital, Minneapolis, or Glen Lake Sanatorium for surgery. Later the Indians were sent to the North Dakota State Sanatorium for surgery from which many Indians were transferred to St. Mary's, Minneapolis, for resectional surgery. Within the past ten years several surgeons qualified in chest work have located in the state.

Many modifications were developed until eventually the Wilms-Sauerbruch-Brauer technique became the most frequent type in vogue. Stage operations certainly reduced mortality. Better technique, better anesthesia, fitting the operations to the patient's condition and respiratory reserve and flexibility of the chest wall all contributed to the safety of surgery. Though still a last resort the indications for surgery were extended to include older and younger patients, to those with contralateral active but not progressive disease, cardiac lesions, and contralateral collapse by pneumothorax, phrenic, pneumonolysis and later even thoracoplasty. A dangerous operation became a very safe one. We reported in 1934 a consecutive series of 208 operations with no mortality from any cause within two months of operation, finally breaking the series when an accidental pneumothorax on the contralateral side followed a postoperative refill. Later Drs. Funk and Larson carried out a consecutive series of 752 operations without any mortality under eight weeks.[120] More than 70% of the patients became sputum-negative and had cavity closure with this procedure.

Although thoracoplasty was for years a last resort, after the early stages of its development it was not a particularly dangerous operation. The entire Glen Lake series 1922 through 1967 on 1,251 patients in 2,976 operations shows there were 45 deaths from all causes within eight weeks of surgery; this is a 3.7% mortality per patient or 1.51% per operation. Patients soon learned not to fear the operation and many begged for it even when totally unsuitable.

The hazards of thoracoplasty were not always confined to the patient. Many years ago in Colorado, Webb brought Edward Archibald of Montreal to Colorado Springs to perform a thoracoplasty on a very ill patient, the wife a very wealthy South American. For several days the husband carried a gun in his pocket with the intention of killing the surgeon should his wife die. Archibald returned to Montreal before she expired.

Thoracoplasty was not uniformly successful,

some cavities did not close, some empyema pockets were not completely obliterated, and some patients did not become sputum-negative. Many factors brought this about, rigid chest, inadequate rib resection or long stumps, delay between stages because of the patient's condition or wound infection. Subsequent revision of the thoracoplasty with or without subscapular packing reclaimed a number of these as reported in a publication by this author in 1935.[205] It was long and rough treatment but did rescue some of the thoracoplasty patients and render them negative.

The results obtained by thoracoplasty were solid and permanent. I still see many of these "old-timers" whose surgery dates from the thirties and later, and have one dating from the fall of 1923. They have lived active, useful lives and many without much handicap. Many have gone through major surgery, pregnancy, pneumonia and other serious illness without difficulty. It was a good operation before something better came along.

With the advent of effective chemotherapy and experience in pulmonary resection, revision of unsatisfactory thoracoplasty was no longer considered, but lobectomy or pneumonectomy was done instead. Pneumonectomies under thoracoplasty were carried out over the years with a low risk.

Drainage of Tuberculous Cavity

Surgical attempts to treat tuberculous cavities have been made for many years. Blegney[32] in 1670 records a case of phthisis cured by a sword thrust puncture of an abscess of the chest. It is unkonwn whether this was empyema or cavity. E. Berry,[25] an Irish surgeon in 1726, reported several cases of direct drainage of tuberculous cavities. Purmann[319] in 1692 advised incision of the chest wall in hemorrhage, empyema, pulmonary cavities and all effusions. Baglivi[14] in 1710 treated wounds of the lung by free incision and advised the same for treatment of tuberculous cavities and cites cases with recovery.

Murphy[283] in 1898 discussed open drainage of tuberculous cavity advising resection of three ribs, drainage with cautery and packing with iodoform gauze. He felt, however, that tuberculosis was a medical not a surgical disease. The results of cavity drainage were not too encouraging so the procedure was avoided for some time until Monaldi[279] in 1938 from the Carlo Forlanini Institute in Italy revived it with his catheter suction drainage.

The new treatment was eagerly accepted by patients and phthisiologist alike and tried in many locations. Some became enthusiastic, other disappointed, in the results obtained. As experience accumulated a number of series were reported. Woodruff[430] of Saranac Lake in 1945 added a Stedman pump for continuous suction and reported on 100 patients treated from 1940, to 1947,[431] feeling it was a salvage procedure as a preparation for other collapse. There was much discussion, many disagreeing with this view. He also reported in 1945 that only four of 13 cavities so treated remained closed after the catheter was withdrawn. Head[361] of Chicago in 1946, also using a Stedman pump suction, reported that after three years only 16 of 29 patients so treated were still alive and that it rarely closed the cavity. L. Davidson[163] in discussion stated that he "hoped this paper was the obsequies of the Monaldi procedure." Monaldi in 1947 stated that there were no dangers in the procedure as an independent operation but that it was more valuable with collapse. Head, Vineberg, Wells and Gardner disagreed and used it only as a salvage procedure.

Monaldi drainage was first established at Glen Lake Sanatorium by Victor K. Funk[120] in 1924 for the relief of cough and to decompress a large tension cavity in the hope that cavity closure might later be obtained by thoracoplasty or other means. The possibilities of complete closure by the treatment alone were not anticipated. Over the next six years, only 14 procedures were carried out on nine patients. No cavity closures were observed, but reduction of cough and cavity size were observed. If thoracoplasty was anticipated at a later date, resection of a couple of ribs under local anesthesia at the site of the proposed catheter insertion was done a couple weeks before the Monaldi procedure so that the later thoracoplasty could be done without entering contaminated territory. No cases were done after 1948. I know of no other series of this type in Minnesota.

Resection for Tuberculosis

The idea of surgical resection of tuberculous lesions had long appealed to both phthisiologist and surgeon, but early results were less than encouraging. Two resection by Kronlein[220] in 1884 ended fatally. Biondi in 1882 experimented on pulmonary resection and recommended it in Tuberculosis. Rugge in 1885 did two cases, both of

whom died. Doyen[89] in 1893 performed a successful partial lobectomy on a 10-year-old girl. Likewise, Macewen removed almost a whole lung for tuberculosis. The patient was well 45 years later. Lowson[253] of London in 1893 resected a right upper tuberculous lesion successfully pulling the lung out through the incision, transfixing it, excising the lesion and later draining an abscess. The patient recovered. Doyen[89] in 1895 again successfully resected a small part of the lung for tuberculosis. Undoubtedly there were other unsuccessful attempts and many tuberculous complications unreported if we can judge from later experience before chemotherapy was available.

Friedlander[115] of Cleveland reported a successful resection of a cavitary right upper lobe for tuberculosis done in 1934. The patient, a 15-year-old girl, had the resection with a Bethune tourniquet and suture using closed drainage. A bronchial fistula developed three weeks later but closed gradually. Leo Eloesser[100] reported having done a lobectomy for bronchiectasis followed by a thoracoplasty for tuberculosis with recovery. Berge[100] reports a case of a pneumonectomy for tuberculosis in 1935 under a thoracoplasty done six years previously with a good result. John Alexander[100] warned against this procedure because of the risks from spread of tuberculosis. A case of mine in 1937, a total pneumonectomy[351] done by individual ligation for a very extensive bronchiectasis with more than 20 negative sputum smears and three negative guinea pig innoculations, was well tolerated but she died of a disseminated tuberculosis six weeks later. The excised lung showed plenty of tuberculosis in spite of the negative tests. What a difference antibiotics might have made.

We carried out a left total pneumonectomy[351] by individual ligation technique without any antibiotic aid in 1940. A nontuberculous empyema requiring catheter drainage and thoracoplasty complicated her recovery. Later silk bronchial sutures were removed bronchoscopically. She enjoys excellent health to date. Two other resections were attempted at Glen Lake but could not be completed because of technical and anesthetic difficulties.

Small series were reported over the next few years but in 1939 Dolley and Jones[87] from the literature were able to collect only 90 cases. Moore[75] by May, 1948, could collect 616 cases with an operative mortality of 15% and a total of 26%. The mortality for lobectomy was higher, 31.5%, than pneumonectomy, 24%, 12% developed empyema. Moore using a prone position reported spreads in 1.6% as contrasted with 14% for other positions. Gale[132] of Madison in 1948 reported a 25% mortality for lobectomy and 45% for pneumonectomy. Overholt in 1947 cited 16% spreads following upper lobectomy and thoracoplasty but 50% where no thoracoplasty was done.

Clagett[384] in 1947 before the Pembine Conference of the Chest Physicians and Surgeons from Michigan, Wisconsin and Minnesota presented a review of his first few pulmonary resections for tuberculosis with favorable results. He was castigated for even attempting to do these. The next year at Pembine Wm Seybold,[384] his associate, presented the continuing series also with good results and few complications, and he in turn was severely criticized for not doing more cases. Ellis.[98] Clagett and Carr in 1951 reported on a 10-year study of 35 cases with upper resection with thoracoplasty with no operative deaths and only one late fatality.

Mass ligation or tourniquet amputation, although used in many of the early resections of the lung, really had no place in tuberculosis resections for it leaves tuberculous disease and probably some necrotic or devitalized lung in the stump. Nearly fifty percent of the patients so treated developed empyema. Although H. Morrison Davies[76] of England did a resection by individual ligation in 1912, it did not become in general use until Churchill in 1931, Rienhoff[326] in 1933, Kent and Blades[200] in 1940, and Boyden[38] in 1945, and others emphasized the segmental anatomy of the lung and the advantages of resection by this method. Fewer complications and a smoother convalescence resulted.

Resections of the lung for tuberculosis before the days of adequate drug therapy could only be carried out with a prohibitive mortality. Dissemination of tuberculosis was the big risk. Under intensive chemotherapy with proper drugs the risk became comparable to that for nontuberculous disease. This became another tool to hasten and make more certain the patient's recovery from tuberculosis.

Locally we had a unique opportunity in the treatment of tuberculosis as the most experienced in the collapse therapy field and in pulmonary resection for nontuberculous conditions. We had the team and equipment to extend these procedures to tuberculosis. With adequate coverage by antibiotics for secondary organisms and now with the newer drugs against the tubercle bacilli a vast field opened up. Glen Lake Sanatorium with 680 beds, the Minnesota State Sanatorium with 240 beds, Nopeming Sanatorium near Duluth with 300 beds, the North Dakota State Sanatorium with 350 beds (40 for Indians), the smaller county or district institutions of Minnesota with 461 beds, the 115-bed Indian service at the State Sanatorium and the large Indian populations of North and South Dakota furnished a large reservoir of patients needing pulmonary resections.

St. Mary's Hospital, Minneapolis, provided adequate hospitalization for patients with tuberculosis under room isolation and had complete operating facilities, anesthesiologist services and trained nursing personnel for postoperative care.

The handling of the surgery for the smaller sanatoria during the period when thoracoplasty was the chief type of operation done from 1936 on was met by referring some to Glen Lake under special arrangements. The others, including those from South Dakota, were admitted to St. Mary's Hospital in Minneapolis under room isolation with stages scheduled ten to fourteen days apart depending on the patient's condition. For several years we kept one wing of thirty beds occupied most of the time. The thoracoplasties for the Minnesota State Sanatorium were done by the author traveling to that institution by car at first, but with gas rationing by train and later by bus every two weeks for two days during which time from three to five patients were operated upon. Most of the work was done under local anesthesia though an anesthetist was also present at the head of the table. The local medical and nursing staffs were trained in postoperative care. The North Dakota State Sanatorium during this period had a local staff trained in thoracoplasty.

When resectional surgery came into the tuberculosis picture, neither of these institutions were equipped to perform this type of surgery. The Minnesota Sanatorium transported its white patients to Glen Lake Sanatorium and its Indian patients to St. Mary's Hospital because they were carried under a different budget. The state-owned ambulance brought two patients at a time accompanied by a trained attendant in addition to the driver. They planned to return in one week with two more patients and return the original pair. With few exceptions this was possible though occasionally if the patient's condition warranted he would be held over for a later trip. The trip was 200 miles each way.

The North Dakota problem was more complicated. The Sanatorium near Dunseith in the Turtle Mountains on the Canadian border was about 600 miles from the Twin Cities. The first 50 miles was by ambulance to Rugby to the Great Northern Western Star train which took them on to Minneapolis where they were met by a local ambulance. This last step became necessary when a couple of Indians disappeared between the train and the hospital into the jungle of bars along Washington Avenue. The police later picked them up. One Indian escaped from the train coming down by diving headlong from the moving car. The track crew found his remains a day or so later. By and large they were good patients once they learned to know the staff and realize that we were trying to help them. Even the children were "dead pan" when first met but later became jolly and liked to laugh and joke.

The Indians presented a unique problem in the Tuberculosis program. Poverty, crowded housing, poor hygienic conditions, alcohol and a restless disposition all contributed to a high incidence of disease. The old idea that they had poor resistance to tuberculosis was disproven by Sanatorium experience which demonstrated that under adequate treatment they controlled their disease just as well as the white patients. It also established the fact that they could not be trusted to take the cure except under close watch—running away for fishing, hunting, pow-wows and other celebrations on the slightest excuse. Both in and out of the sanatorium they could not be depended upon to take the drugs prescribed so that prolonged chemotherapy was out of the picture. The above facts precluded the use of pneumothorax and other temporary procedures. Our program then called for thoracoplasty and other permanent procedures in the early days and intensive chemotherapy followed by resection of any cavity or dense lesions which did not respond rapidly and completely. The Indians were from

Minnesota, North and South Dakota and a scattering from Iowa, Wisconsin, Montana and Wyoming. The tribes included: Chippewa or Ojibway, Dakota or Sioux, and a few Menominee, Potawatomii, Oto, Sauk Fox, Arikara or Ree, Mandan, Absoraka or Crow, Cree, North Cheyenne, Shoshoni, and Arapaho. Over the years we have done resections on over 250 Indians.

An occasional language barrier was encountered among the older patients but they were usually sent down with another patient who could translate for them. The children were usually accompanied by a nurse from the home sanatorium. A few inmates from the state prison came with a guard but none caused any trouble. Most of the Indians tolerated their surgery very well and obtained good results, often in spite of themselves. Removal of the infectious ones from the community and eliminating the open cavities reduced the spread of the disease. The Indian building at the State Sanatorium has been closed now for a number of years.

Chemotherapy

The early history of antibiotics in the Twin Cities is largely the studies and reports of Wesley Spink[38] of the University of Minnesota. He introduced sulfa drugs to this area in 1937 and did extensive studies with them. In 1942 he did the same with Penicillin. His extensive studies with both drugs clearly defined their valuc, indications and reactions.

The early history of the anti-tuberculosis drugs, both locally and nationally, stems from the Mayo Clinic and the Mineral Springs Sanatorium at Cannon Falls. William Feldman, a veterinarian from the Experimental Institute at Rochester, Corwin Hinshaw of the Chest Department of the Clinic, and Karl Pfuetze,[310] medical director at the Sanatorium, became the team which studied, experimented and evaluated the experimental drugs as they became available for animal use and later applied them to patients. Promine was studied in 1941, Diazone in 1943-44. They were the first to report that it had little if any effect on clinical tuberculosis and did have serious toxic potentials. Promizole which worked well in guinea pigs was proved of no value in clinical tuberculosis. Streptomycin discovered by Schatz in 1944 and Para-aminosalicylic Acid (P.A.S.) by Lehmann in 1946 were studied in combination by this group in 1947-48. The preliminary laboratory and guinea pig work on all the drugs was done by Feldman who was most enthusiastic in his studies. This was not an individual project but rather a group study of many men from the Mayo Clinic including. Corwin Hinshaw, Davc Carr, Herman Moersch, Arthur Olson and Herbert Schmidt from the chest section, O. T. Clagett and William Seybold from chest surgery, Al Brown from ear, nose and throat, William Bickel, Paul Lipscomb, Mark Coventry and Herman Young from orthopedics and other consultants in neurology, urology and anesthesiology. For all the time, thought and effort expended by this group in this study, not a single one would accept a single penny in compensation, not even for the gas burned in the numberless hundred-mile round trips to the Sanatorium.

A 20-year-old girl in 1924,[88] became the first to receive an injection of Streptomycin. The first case of spinal tuberculosis to be treated anywhere with Streptomycin was also a patient there, the drug bringing about healing of tuberculous sinuses on the back permitting a surgical fusion to be carried out by Bickel.[88]

New antituberculosis drugs were thc result of extensive studies by many investigators. Oxytetracycline was reported by Bernstein in 1950-51; Isonicotinic Acid Hydrazide (I.N.H.) by Yeager, Benson and Fox in 1951; Viomycin by Finlay in 1951; Pyrazinamide, a synthetic by Kirschner, in 1952; Cycloserine by Harned and by Epstein in 1955; Ethambutal discovered in 1951 was released for clinical use in 1968. Cooperative controlled studies under the U. S. Public Health service were carried out in 22 institutions, including Glen Lake Sanatorium and the U. S. Veterans Bureau Facility in this area on large series of patients in order to evaluate the ability of separate as well as combined programs to control tuberculosis in new, retreatment and resistant cases.

The impact of ordinary antibiotics upon medicine and surgery can scarcely be realized. Many diseases were promptly controlled and others improved. Surgical infections were reduced or more easily controlled. The tuberculosis field was even more favorably influenced. Tuberculous meningitis which previously had been almost 100% fatal now could be controlled. Pulmonary tuberculosis, even extensive disease, may be effectively arrested in one-third the previous time

period and with more certainty. Surgery, especially resections, became much safer and paradoxically the indications much fewer. As a result the sanatoria developed vacancies in place of waiting lists and all but four in the state were converted to other use. The prophylactic use of INH in children and recent tuberculin converters has now become common practice. The U. S. Veterans Bureau Hospital and Armed Services Group studies on Tuberculosis and malignant disease has aided materially in the better utilization of the available drugs.

Traumatic Rupture of the Bronchus

Traumatic rupture of the bronchus or trachea is an uncommon but very serious type of injury. First reported by Winslow[428] in 1871 as a healed lesion found in a wild canvas-back duck, Seuvre[367] reported the first human case in a human fatally injured in 1873. The next 18 cases to be reported were all fatal until Krinitzki[218] in 1928 reported the case of a woman who died of pulmonary tuberculosis 21 years after a severe chest injury. The right main bronchus was completely obstructed with no evidence of tuberculosis in that lung. Subsequent to 1942[209] there were twelve patients who recovered slowly after decompression of the tension pneumothorax, the lung remaining atelectatic. All of these patients had sustained severe crushing injuries to the chest with or without rib fracture. The bronchial injury was usually a clean transverse section of the main bronchus close to the trachea, with the vessels intact. Rarely a similar section occurs in the trachea. The occurrence of this lesion should be suspected after a serious crushing injury with pneumothorax and cough with a little blood with or without mediastinal emphysema. Decompression of the pneumothorax followed by bronchoscopy will establish the diagnosis.

The first recorded case from Minnesota was reported by Jones and Vinson[189] of the Mayo Clinic in 1939 with bilateral pneumothorax aspirated repeatedly with recovery leaving a stenotic left main bronchus and atelectasis. The three patients[209] with stenosis and atelectasis whom we have seen recovered when treated as above. One subsequently had a pneumonectomy when the lung became infected. Another patient with bilateral tension pneumothorax and a fractured bronchus on the right survived with bilateral suction catheters. The bronchus was wide open and in good position for healing. In spite of all efforts to keep it patent with a seton and bronchoscopic dilatation, it went on to complete obstruction and atelectasis. Metastatic malignancy ended the picture without any further surgery. The ideal treatment after early diagnosis as soon as the patient can tolerate thoracotomy is to expose and do a primary suture of the bronchus or trachea.

N. K. Jensen[185] in 1953 successfully repaired a fractured bronchus at the Minneapolis General Hospital and later that year repaired a fractured trachea. He also repaired another bronchus at Northwestern Hospital[293] in 1949 and another in 1960.

Late excision of the stenotic area in the bronchus and direct anastomosis has been done and followed by re-expansion and function of the lung.

Chest Tumors

Tumors of the chest and mediastinum undoubtedly were more common than were recognized because many, especially those of an intrathoracic position, gave few or no symptoms until they reached some size or interfered with some structure. Hedblom[165] of the Mayo Clinic in 1921, totaled the reported cases at 213 to that date. He presented a very complete review of the subject with an extensive bibliography. He quoted von Speicher[379] of 1881 as collecting 28 cases, Parham[302] of New Orleans in 1898 with two cases of his own and 101 collected cases, and Lund[255] in 1913 adding 27 additional collected cases and one of his own. Hedblom in this report added 35 more cases from the literature, added 23 operated cases from the Mayo Clinic since 1910, and an additional 25 cases from the Mayo Clinic in which no surgery was done, for a total to that date of 213. From this group 62.8% were sarcoma and 8% chondrosarcoma; 167 or 78.7% involved the ribs, and 41 or 21.3% the sternum. He demonstrated one case of a melanoepithelioma of the manubrium operated upon twice but lost after six months from the recurrence. He quoted Parham[302] for crediting Oaias Aimer with the first thoracotomy for tumor in 1778.

Carl A. Hedblom[168] in 1933, then in Chicago, reported on intrathoracic dermoids and teratoma

collecting 185 cases from the literature and adding six personal cases. S. W. Harrington[156] reporting from the Mayo Clinic in 1929 on surgical treatment of intrathoracic tumors, added 12 to the five he had listed previously; 15 were completely removed, eight were malignant. By 1931 he reported on 28 cases in the lung and mediastinum, 14 were malignant and 14 benign. He later listed 11 cases of intrathoracic teratoma in five years, ten in the mediastinum and one above and below the diaphragm. The relatively small size of these series in comparison to the Mayo Clinic' volume of cases registered emphasizes the relative infrequency of these tumors.

Kronlein of Zurich in 1884[220] reported the removal of a tumor of the chest wall and attached lung from an 18-year-old boy who recovered and was apparently well two years later.

The earliest local record of intrathoracic tumor we have been able to find was presented before the Minnesota Academy of Medicine, 1888, by J. Clark Stewart.[387] It was a huge anterior mediastinal tumor displacing the sternum and obstructing the mediastinal structures. It was not amenable to surgical removal. It proved to be a small-cell sarcoma at postmortem examination.

With the advent of statewide chest x-ray surveys in Minnesota in 1946-48 and in North Dakota in 1946, South Dakota from 1949 to the 60s and routine hospital chest X rays, many unsuspected and usually asymptomatic tumors of various kinds were discovered. These surveys over a period of time brought to us, referred from physicians throughout the territory, a large number of chest tumors numbering well over three hundred. The most frequent tumor of the anterior mediastinum was the teratoma and its dermoid variety while posteriorly it was the neurogenic tumor. These tumors form the basis for my book, "Tumors of the Chest"[211] published in 1963. The charts, copies of Xrays, Kodochromes of specimens, and tissue sections are preserved in a special section of the medical Library at St. Mary's Hospital in Minneapolis. I did the photography.

Bronchogenic Carcinoma

Bronchogenic carcinoma, that perennial mimic of the pathological field which has been present long before it was recognized, still masquerades as pneumonia, viral pneumonia, tuberculosis and a variety of other conditions. Unrecognized as cancer amongst the Schneeberg miners of Uranium ores in the middle ages, it was first proven pathologically by Morgagni[280] in 1761. Bayle in 1810 first described cancer and tuberculosis in the same patient. Laennec later was able to differentiate the two conditions. Bell in 1846-7 was the first to make the clinical diagnosis of a primary lung tumor though it was later called a sarcoma, a diagnosis which even today may be open to question. The pathological studies of Rokitansky[342] and Virchow aided in the differentiation from other lung conditions. The monograph of Adler[2] in 1912 was the first extensive American publication on the subject. He listed 374 collected cases and called it forcibly to the attention of clinicians, in spite of which it was rarely considered in differential diagnosis.

Moses Barron[20] from the pathology department of the University of Minnesota in 1922 reported that 13 cases were found in 4,362 postmortem examinations, an incidence of 0.29%. The Minneapolis General Hospital reported 14 cases diagnosed in 1935-39 from 26,301 patients registered, an incidence of 1 per 1,878 admissions (0.53%)

The question must arise as to how many cases were unrecognized. I well recall while an intern at the Minneapolis General Hospital in 1919 three cases which came to postmortem examination presenting extensive carcinomatosis with metastasis to liver, adrenal and other organs plus a lung lesion. They were signed out as carcinoma, primary site, probably liver or bile ducts because of the extensive liver involvement.

Glen Lake Sanatorium[131] from 1916 to 1939 reported 17 cases from 6,343 admissions, an incidence of one in 373 patients who for admission must have had at least a tentative diagnosis of pulmonary tuberculosis in order to be received. Even in 1941 at the chest service conference of the Veterans Facility, the reaction when a suggestion was made that a certain case might be carcinoma instead of tuberculosis was that carcinoma was a very rare disease which they never encountered. The publication of Edwin J. Simons' book, "Primary Carcinoma of the Lung,"[374] in 1937 did alert the local profession to this disease. Simons, a rural practitioner from the small town of Swanville, Minnesota, (population 435) became interested in the subject because of the

occurrence of two cases in his practice within two years, one a 19-year-old boy.

One of the most important requisites to making a diagnosis of bronchogenic carcinoma is a high index of suspicion and tenacity in following through to establish the diagnosis or rule it out. A battery of special tests may be necessary including some of the following: Xrays, planigrams, cytology studies on sputum and bronchial washings, bronchoscopy and biopsy, prescalene or mediastinal node biopsy.

Its surgical treatment is of recent origin. Kronlein[220] in 1884 reported resecting a section of the chest wall and attached lung in an 18-year-old girl who was apparently well two years later. I suppose this diagnosis might be questioned. Kummel from Germany in 1910 carried out a pneumonectomy for carcinoma by mass ligation but lost the patient on the sixth day. H. M. Davies[76] of England in 1912 did a lobectomy for carcinoma by individual ligation, the patient dying on the eighth day from empyema. He advised exploratory thoracotomy.

Adler[2] in 1912 could collect only 211 cases before 1900. Sauerbruch[355] in 1920 reported two cases of partial resection. Lillienthal[247] in 1924 resected a lobe but preferred pneumonectomy. Allen and Smith[7] in 1930 reported a patient who lived four years following a lobectomy for carcinoma. Tudor Edwards[94] of England in 1932 reported good results in a case of squamous carcinoma with a small excision followed with Radon implantation. Later the growth was gone. Churchill[56] in 1933 reported a lower and middle lobe excision for carcinoma. Reinhoff[326] in 1933 reported two pneumonectomies by individual ligation through an anterior approach. Reinhoff and Broyles[327] in 1934 reported resecting one carcinoma and one sarcoma with good results. Egger[27] in 1934 reported one lobectomy. Rabin and Neuhof[323] reported five lobectomies, one of whom was alive one year later. Archibald reported two with good results. Young had one left upper lobectomy patient who was well one year later. Andrus[11] in 1935 reported six cases treated by cautery excision with three alive two, two and one-half, and three years later. Evarts Graham[141] of St. Louis carried out the first successful total left pneumonectomy for carcinoma in the United States on April 3, 1933, doing a mass ligation excision and a concommitant thoracoplasty. The patient, a physician, not only recovered but resumed practice and outlived his surgeon. Overholt[299] later in 1934 reported the second successful pneumonectomy in America and in 1935[300] recorded 13 patients so treated, seven for metastatic disease and six for primary carcinoma with three recoveries. Bigger[27] in 1935 reported one successful lobectomy and one pneumonectomy patient who died of suppurative pericarditis. Ochsner[294] on April 15, 1936 reported his first case, the tenth successful one on record. Churchill[57] in 1937 recorded three total pneumonectomies. Reinhoff in this same year added six more cases. Churchill[57] in 1938 added a conservative view to the picture showing that lobectomy often gave as good results as pneumonectomy and with a smaller risk. Allison[9] of England in 1950 presented a more radical view advocating radical pneumonectomy rather than the ordinary operation in spite of its increased risk and complications.

Harrington[161] from the Mayo Clinic in 1935 after a preliminary thoracoplasty did a pneumonectomy for carcinoma; unfortunately, the patient died postoperatively of respiratory and cardiac failure. In 1937, at Northwestern Hospital I carried out a left total pneumonectomy by individual ligation on a 62-year-old man for squamous cell carcinoma for the first successful pneumonectomy for carcinoma in Minnesota. His convalescence was uneventful and he lived 13 years and nine months, dying of hypertensive cardiovascular disease without any evidence of recurrence. Harrington[161] in 1941 made a report of the Mayo Clinic to that date listing 31 cases, of which 21 were explored and found non-resectable, nine had pneumonectomy in one stage, three dying after surgery with five alive at three to eighteen months after resection. Brindley[58] and Clagett in 1943 reported 95 cases explored with 45 resected. The mortality from pneumonectomy was between 10 and 15%. Geha, Bernatz and Woolner[126] from the Clinic in September, 1967, reported that of 2,113 patients with bronchogenic carcinoma explored, 174 had tumor invasion of the chest wall, in 14 of whom the involved area was resected in conjunction with the involved lung. N. K. Jensen[186] in discussion mentioned that of 1,000 cases collected from their files, 700 were explored and 475 resected, and that of 18 who had chest wall invasion resected, six survived for five years.

John C. Jones et al.[191] in 1967 reported that in

the United States in 1967 it had been predicted that 42,000 males and 8,000 females would die of lung cancer. He also stated that of 358 patients resected between January, 1937, and July, 1967, there were 94 patients who survived five years, 264 died within five years, an average survival of 13 months. Before 1950 all patients had pneumonectomy, later 30% had lobectomy; the operative mortality was 1.7%, the thirtieth day mortality, 6.2%. Overholt[301] in discussion listed 2,657 cases with 70% explored, 49% resected. There were 191 five-year survivals, 91 by pneumonectomy, 79 by lobectomy and 21 by segmental resection.

The long term prognosis from bronchogenic carcinoma is always uncertain. The author recalls one patient,[351] a 71-year-old hard rock miner with extensive silicosis and a squamous cell carcinoma of the left lower lobe. A left lower lobectomy was done. The local lymph nodes were involved with carcinoma, a hard mass in the lower mediastinum could not be removed. He not only recovered but survived for twenty years, dying from Cor pulmonale without recurrence. Did silicosis block the lymphatic spread of his tumor?

Mediastinoscopy and Pre-Scalene Node Biopsy

Daniels[74] in 1949 described a new method of biopsy useful in certain types of intrathoracic disease. It consisted of excision of the fat pad and lymph nodes overlying the scalene muscles in the low cervical region. Confronted with intrathoracic disease with a suggestion of possible mediastinal lymph node enlargement it offers a chance of obtaining tissue for microscopic diagnosis for the lymphatics in the prescalene have a direct connection with those of the mediastinum. The finding of carcinoma in the lymph nodes in this area would prove the noncurability of a carcinoma of the lung and the futility of resecting the lung lesion with any hope of cure. Tissue obtained from this region may establish a diagnosis of sarcoid the most common finding, or tuberculosis, silicosis, or lymphoma. Slowly it became accepted and later became widely used. It is a low risk procedure which often furnishes valuable information.

Dwight Harken[153] of Boston in 1954 described a simple cervicomediastinal exploration for tissue diagnosis of intrathoracic disease. Through the same incision used for prescalene biopsy, he inserted a finger into the upper mediastinum, dissecting the loose tissues anterior to the trachea and through a small laryngoscope visualized, aspirated and biopsied or excised lymph nodes deep in the mediastinum. He had done over 300 such operations at the time of his report, encountering bleeding easily controlled with gelfoam and a small pneumothorax on two occasions. Positive carcinomatous nodes were obtained in 85% of cases of bronchogenic carcinoma.

Eric Carlens[48] of Stockholm, Sweden, in October, 1959, described a similar procedure carried on through a small transverse incision in the midline just above the manubrium under local or general anesthesia. R. Rynders[346] of Amsterdam in June, 1964, reported on 250 such procedures since 1960 with only two complications, a right recurrent nerve interruption and one instance of bleeding easily controlled by packing. Carlens in 1964[48] reported the method 94-100% accurate in sarcoid. A number of local thoracic surgeons and bronchoscopists are now doing the procedures. Duval, Johnson and Koop[188] of Minneapolis in July, 1968, have reported on over 100 cases with no complications. Pearson[307] of Toronto has recently given an evaluation of Mediastinoscopy in the management of presumably operable bronchogenic carcinoma.

Surgery of the Esophagus

The esophagus presents a number of conditions which may require surgery.

Foreign Body

Many of the foreign bodies in the esophagus may be removed endoscopically and have been considered under that heading. William Lerche of St. Paul in 1911 discussing foreign bodies in the esophagus warned against passing sounds to dislodge the offender. He stated that if perforation has occurred in the cervical region, one should not esophagoscope, if in the thorax one should pass the scope to determine the site of the abscess. He quoted Kohn as collecting 326 cases of cervical esophagotomy with a mortality in 1880 of 26% and from 1900-03 of 12.6%.

Perforation

Perforation is always a possibility with foreign body or even with the passage of a scope and can be a very serious condition. When I first joined the surgical staff of the Minneapolis General Hospital in 1936, there had been no recoveries following perforated esophagus. Over the next few years we operated upon seven pa-

tients with cervical perforations losing only one before the days of antibiotics. This man died of a brain abscess several days postoperatively. His perforation was over 24 hours old when he was first seen.

Pharyngeal Diverticulum—Zenker's Diverticulum

Pharyngeal diverticulum, often called Zenker's Diverticulum, although Ludlow[254] in 1764 first described the condition, is really a herniation of the pharyngeal mucosa through a weak spot or defect in the midline just above the cricopharyngeus muscle, the Lannier-Hackerman area. Rokitansky[342] in 1840 described the condition and suggested dilatation for treatment. Nichaus[289] in 1881 is credited with the first extirpation. C. H. Mayo[267] in 1910 reported eight cases with one and two stage operations, with two postoperative fistulae and warned of the danger of aspiration during operation. He mentioned one case with a sac which held sixteen ounces of fluid. This author had one patient a number of years ago who was referred in as a mediastinal tumor but whose diverticulum extended into the upper mediastinum and held over a pint of barium. DeWitt Stetten[385] in 1910 stated that Kluge in 1894 suggested excision. The earlier operations included invagination of the sac, elevation and suture of the sac to facilitate drainage before secondary excision and two stage excision. Soon, however, only the one stage resections were done and many general surgeons were doing this type of work.

Pulsion diverticula in the lower third of the esophagus are seen occasionally and in the absence of symptoms and obstruction at the cardia are usually not treated. When necessary they may be excised through a left low posterior thoracotomy in one stage by a similar technique to that used in the cervical region.

Traction diverticula usually found in the mid esophagus result from drainage of a suppurating lymph node into the adjacent viscus. If necessary, which is rarely, they may be treated by excision of the adjacent nodes and suture of the fistulous tract.

Achalasia of the Esophagus

This condition was first described by Purton[320] from the postmortem findings in 1821. Megaesophagus of achalasia, a term introduced by Hurst, should replace cardiospasm as formerly used because the condition is due to a disturbance in motility of the involved organ rather than a spasm of the local esophagogastric junction. The broadening of the mediastinal shadow seen on single x-ray films is frequently confused with tumor though the differential diagnosis is not difficult. Various treatments have been suggested, none of which is completely successful. Dilatation by passing small bulb dilators over a string guide rarely produces lasting relief. The use of the string guide was to Mixter's credit; was used by many (Plummer,[315] Vinson,[410] Lerche and others,) and added much safety to many intraesophageal maneuvers. A number of types of dilators for use in the esophagus were devised over the years, the mercury-filled Hurst type,[180] the Kohlman of Lerche, the air pressure dilator of Mosher and Sippy, the Mosher mechanical dilator and the Russell dilator of the hydrostatic type improved and used extensively by Plummer and Vinson[411] and their group. The forceful stretching of the narrowed area by the hydrostatic dilator afforded lasting relief to at least 75% of the patients so treated. The dangers of perforation were ever present but by first dilating to 60 French before using the hydrostatic dilator, the risk is materially reduced. Vinson[411] reported no fatal outcome in over 450 patients so treated. The operation of esophagoplasty suggested by Wendell in 1909 using a longitudinal incision of the narrowed segment followed by transverse closure may provide drainage to the dilated esophagus but may be followed by distress from regurgitation and at times corrosion esophagitis. More recently the Heller esophagotomy operation on the lower esophagus has come into favor in place of the older procedure. Sweet[390] in 1956 divided cases of achalasia into two groups. Type I (75%) show enormous dilatation of the esophagus with little peristalsis with a small lower segment with thin muscle layers. Type II (25%) show only moderate dilatation with active to hyperactive peristalsis and even reverse peristalsis with a thickened lower segment with hypertrophy of the musculature. Both show degeneration of the ganglion cells in the wall. Forceful dilatation or an esophagogastrostomy gives best results in Type I. Type II does better with an esophagotomy.

Esophagus

Spontaneous Perforation

So called "spontaneous rupture of the esopha-

gus" was first described by Boerhaave[35] in 1774 and over fifty cases were collected by a number of authors including Barrett[19] in March, 1946, and Eliason and Welty[97] in August, 1946. A report[210] on this condition in 1948 covers the whole picture and a complete record of the literature to date, together with a record of the five new cases seen to that date in Minneapolis.

The clinical picture, while not well recognized even to this date, is so characteristic that it has been diagnosed at least twice over the telephone, once by Wangensteen and once by this author. The first patient, at the St. Barnabas Hospital[210] died undiagnosed thirty hours after the onset and twelve hours after an exploratory laparotomy for suspected perforating ulcer. The second, a 16-year-old boy with poliomyelitis with severe repeated vomiting, also died without the diagnosis being made until the postmortem examination. A third case was diagnosed, the tension pneumothorax and pleural fluid removed, but in spite of supportive measures his condition never improved sufficiently to permit surgery. A fourth patient was seen nearly two and a half weeks after the onset of trouble, in desperate condition with left pleural effusion. The diagnosis was made; the chest decompressed and the fluid removed. His condition would not permit surgery although it was considered. The family decided to take him to Rochester where he had been a patient on several occasions. He died two hours after arrival. Postmortem examination revealed a longitudinal tear in the lower third of the esophagus. The fifth patient,[210] 67 years old, collapsed on the street and a few hours later was brought to the General Hospital in shock and very dyspneic. The diagnosis was made over the telephone while talking to the resident. He was operated upon promptly; over a quart of old food removed from the left pleural cavity and the esophageal rent sutured. Convalescence was stormy but he improved until the ninth day when he died of a pulmonary embolus. Two other cases were observed later with one recovery following early surgical repair, the other under antibiotic therapy without surgery. Drs. Olsen and Clagett[296] reported one patient in 1947 who was operated upon early with recovery.

One important fact has been learned in treatment of this catastrophe. Diagnosis must be prompt and thoracotomy carried out at once without waiting for supportive measures to bring up the blood pressure. Decompression of the tension pneumothorax, evacuation of the food and acid from the chest and washing the irritating material from the pleural cavity will be followed by return of the blood pressure while the surgery is in progress. The esophageal rent should then be sutured, and the chest closed with suction catheters. Antibiotics have improved the prognosis very materially. A review by O'Connell[295] of England in 1967 carried an extensive reference list.

The experimental reports of Wangensteen[421] and his group would seem to indicate that pyloric obstruction with regurgitation of the highly corrosive acid-pepsin stomach contents in the lower esophagus so weakens its wall that the force of the vomiting splits the wall in a longitudinal manner.

Esophageal Atresia and Tracheo-Esophageal Fistula

This condition was first described by Thomas Gibson in 1696, and was almost universally fatal until 1939. N. Logan Leven[238] of St. Paul in 1935 and 1936 operated upon two babies, the first, a four-day-old, first doing a gastrostomy with obstruction of the cardia by catheter. At a second stage cervical esophagostomy was done, connected to the gastrostomy by an external tube. The child died on the 98th day. The second done by a somewhat similar technique survived over 53 days.

H. M. Richter[328] in 1913 through a transpleural approach with a gastrostomy below had ligated the fistula using a mechanical respirator made with an old vacuum cleaner motor. The patient did not survive. Robert Shaw[369] of the University of Michigan in 1938 ligated and divided the fistula and made a primary anastomosis of the esophageal segments. The patient died on the 12th day. Paul Samson[348] did a similar case. Lamman[230] in 1936-37 did four cases by an extrapleural approach with primary anastomosis and another in 1939; all died though two lasted eight to nine days. Cameron Haight[151] of Ann Arbor, Michigan, five months after the Shaw report did a primary repair, the baby dying seventeen hours later. Within the next 23 months, two more were done by him and two by John Alexander,[4] but all died. They did not know then of the work of Leven and Ladd.

N. Logan Leven[240] in 1939 did the first successful treatment of tracheal-esophageal fistula with an initial gastrostomy and occlusion of the cardia. He then did an extrapleural approach with closure of the fistula and did a cervical esophagostomy. Much later a tube reconstruction was done. Ladd[226] later did tube reconstruction. Sweet[391] preferred reconstruction by bringing the stomach into the chest for anastomosis. Potts and De Boer[77] in 1946 reported four operations with 100% mortality. Ten years later[77] they reported 117 patients, doing a transpleural exposure, a two layer closure and without gastrostomy. By 1952 at the University and Ancker Hospitals, Leven, Varco, Lannin and Lyle Tongen[241] reported 103 cases.

Tague Chisholm[54] of Minneapolis did his first tracheo-esophageal fistula operation in 1947 and subsequently to 1968 has done 161 cases, losing 22 or 13.7% mortality which is remarkable considering the desperate condition of some of the babies when they arrive from distant sources.

D. J. Judd, Clagett, Havens and Moersch[194] of the Mayo Clinic in 1944 reported a man of 30 with an acquired fistula from a bullet wound cured by a two-stage operation. The total Mayo Clinic series 1916-65 was 36 cases. Wychulis,[432] Ellis and H. Anderson reported 14 cases since 1948 with 13 of 14 having an uncomplicated recovery.

The reviews of this subject by Anderson and Sabiston[10] in 1965, Sacks et al.[347] in 1965, indicate that the condition is not as rare as formerly supposed and can frequently be successfully repaired.

Carcinoma of the Esophagus

Carcinoma of the esophagus has posed serious problems to the medical profession for a long time. The slowly starving patient came, hoping for relief, which the doctor could not provide. Gastrostomy for feeding was poor palliation for though it provided for some nutrition, it afforded no relief from the continuing saliva and other secretions which were the most distressing part of the obstruction. Also, when used in the very debilitated patient it carried an appreciable mortality from lung complications from aspiration of secretions. Dilatation by means of graduated bougies passed over a string guide and repeated every few weeks often kept the strictured area open sufficiently to permit passage of liquid and soft food as well as saliva and secretions, until the patient succumbed to metastasis. Plummer[314] and Vinson,[410] Lerche[242] and Schwyzer[365] from this territory used this method for many years and contributed much to the handling of these unfortunate individuals. Adolf Kussmaul[223] in 1868 is credited with being the first to directly visualize a carcinoma of the esophagus by means of an endoscope. A. Schwyzer[365] of St. Paul also visualized carcinoma of the esophagus, made biopsies of it and used radium.

Vinson and Moersch[409] in 1925 stressed the relative safety of dilatation in carcinoma, three deaths in 502 dilatations contrasted to at least a 10% mortality for gastrostomy. Souttar[377] of England in 1924 developed his spiral German silver tube for intubation of the strictured carcinomatous area to permit feeding and swallowing of secretions. Symonds[392] and dePezzar tubes were also used.

Radiation for Carcinoma of the Esophagus

Radiation treatment for carcinoma of the esophagus has been tried by many since radium was first introduced, with varying results. We know that Arnold Schwyzer[365] of St. Paul used it as early as 1904. Deep therapy has been known to relieve the obstruction to a rather marked degree but was followed later by a marked stricture resistant to dilatation. Nakayama[286] in 1967 reported three of eight patients surviving over five years following radiation and surgical removal but does not state whether there was any node involvement, a most important consideration. Groves[147] of Cleveland in 1968 reporting on combined treatment of 37 patients with carcinoma of the esophagus and cardia, notes that 21 were adenocarcinomas, 13 were squamous and two undifferentiated carcinomas. The long survivors, 18-36 months, were all in the group without node involvement.

Theodor Billroth[28] in 1872 is credited with the first successful total resection of the stomach and lower esophagus for carcinoma. Mikulicz[276] in 1886 was the first to treat carcinoma of the esophagus by resection and plastic reconstruction. The patient died.

Carl Schlatter[362] of Zurich, while on a locum tenens for Prof. Kronlein in 1897, did a complete gastrectomy, the specimen showing duodenal tissue on one end and esophageal tissue on the other. He anastomosed the jejunum to the esophagus. The patient died 15 months later from recurrence.

Kendell Franks[112] is reported to have resected a localized nonmalignant stricture of the esophagus and performed an end-to-end anastomosis over a tube before 1899. Sir Berkeley Moynihan[281] of England in 1903 is reported to have done a total gastrectomy. Voelcker[412] in 1908 is reported to have anastomosed the esophageal stump to the jejunum after removal of the stomach. W. J. Mayo[268] in 1917 did a total gastrectomy and removed 16 mm. of the lower esophagus. Patient recovered and was doing well five years later. Hedblom[166] in 1922 in a two stage procedure resected the stomach for carcinoma of the cardia with 4 cm. of the esophagus; the patient surviving over five years. He first did an extensive lower left thoracoplasty, then later resected the tumor, bringing the stump of the esophagus out to the skin in the mid axilla and connecting it to a gastrostomy opening by means of a rubber tube.

These cases were undoubtedly cases of high gastric carcinoma and not primary carcinoma of the esophagus. Many others were probably attempted unsuccessfully.

Graham and Ballon[139] in 1931 stated there were no survivals of carcinoma of the lower third of the esophagus operated by the abdominal route. Franz Torek[396] of New York in 1913 performed the first successful resection of carcinoma of the thoracic portion of the esophagus. A gastrostomy was done first, then after resection of the anterior portions of ribs four through seven, the entire esophagus was resected bringing the cervical portion out through the skin. This stump was then connected to the gastrostomy opening by an external tube. Lillienthal[246] in 1920 using a new technique without a gastrostomy excised the tumor and joined the esophageal stumps by an extrapleural skin tube for the second successful case. Carl Eggers[95] in 1924 performed the third successful resection bringing the upper segment out through the neck, tunneling it to the second interspace subcutaneously from which an external tube was led to the stomach.

Dissatisfaction with the Torek type of procedure led to the development of a number of procedures to obviate the external rubber tube connecting the upper esophagus and the gastrostomy opening. For carcinoma of the pharynx and cervical esophagus Gluck[133] and Wookey's[429] operation involving excision of the tumor plus the larynx and construction of a skin tube to bridge the gap became standardized. For carcinoma of the lower third of the esophagus excision of the tumor, mobilization of the stomach through the diaphragm and anastomosis of the esophagus to the stomach elevated into the chest offered a one stage answer to the problem. Carcinoma of the remainder of the thoracic esophagus posed more serious difficulties. The stomach, jejunum and right colon were used to establish continuity. Yudin[436] and others in their articles illustrate many of the reconstructive procedures. These were placed intrapleurally, through an anterior mediastinal tunnel or through an anterior subcutaneous tunnel. Anastomotic leakage, infection and loss of blood supply to the transplanted segment, stricture and regurgitation were not uncommon. Infection was more serious in the intrapleural than in the subcutaneous area. Prognosis was related to the late stage of discovery, the amount of lymph node involvement and position of the tumor. The number of five year survivals was never great.

Surgery for carcinoma of the esophagus in the early days was not only hazardous but the results were far from encouraging. At the Minneapolis General Hospital,[278] 1940-47, we explored ten patients with involvement by squamous tumor. All were emaciated and in poor condition. Three were nonresectable. Six were resected using the stomach for re-establishing continuity, two well above the aortic arch. Three survived but died of metastases within the year. Three succumbed to infection and leakage of the anastomosis. Such results were discouraging so the procedure was not pushed. Phemister and Adams[1] of Chicago in 1955 reported on 475 patients with carcinoma of the lower esophagus and cardia seen between January 1, 1945 and December 31, 1952; 210 were inoperable, 256 were explored and 125 resected. The hospital mortality was 16.7%. Eleven survived five years. Among the 219 patients who were inoperable 88% were dead in one year and 97% in 18 months. Terracol and Sweet[391] in 1958 reported 20% survival in five years from cervical carcinoma, zero for superior mediastinal tumor, 23% for mid-thoracic tumor and 32% for lower segment carcinoma. Dietrich,[84] Dockerty, Olsen and Ellis from Rochester in 1963-64 discussing the lower segment tumors, reported seven of 13 squamous cell carcinomas survived more than five years, with only 13 of 120 adenocarcinomas alive in five years. Although much has been ac-

complished over the years in spite of many discouraging experiences and much reason for pessimism, it is well to remember that every one saved is truly a brand from the burning.

Wangensteen[422] and his staff of the Surgical Department at the University of Minnesota Hospital became interested in this problem in the late thirties or early forties, and soon encountered the same complications which others had found, but characteristically they turned to the laboratory for their answers. Esophagitis, leakage, poor healing, ulceration, stricture, hemorrhage and perforation were the result of acid-peptic digestion from regurgitation of stomach contents which could not move on because of pyloric closure following the vagotomy incident to mobilization of the stomach and esophagus. Pyloric myotomy or pylorotomy plus partial gastric resection were soon added to the procedure to correct the situation. Retrograde suction through the duodenum to keep the stomach empty of acid secretions and a jejunostomy feeding tube to supply nutrition to the very debilitated patient were well worthwhile. They came to a mid-sternal approach to the right pleural cavity for the reconstruction. Later the right colon was considered a better replacement for the esophagus than the stomach or jejunum. By 1956 they had five patients surviving and apparently well six or more years following resection for lower third tumors.

The recent report of Humphrey and Clifton[178] from Memorial Hospital in New York reviews their entire series of 592 patients seen from 1926 to 1961 and includes both epidermoid and adenocarcinoma; 154 patients received no treatment or only gastrostomy; 188 or 31.4% received irradiation; 387 or 65% were explored, and 243 or 41% underwent resection; 17 patients with epidermoid tumors were treated by colonic bypass with a 5.5% mortality. No untreated patient survived more than two years and only 16% more than six months. All untreated patients with epidermoid tumors were dead within ten months. The operative mortality for resection for epidermoid carcinoma was 21.6% while that for adenocarcinoma was 27.1%. The long term survival for resected epidermoid carcinoma with positive node involvement was 28% for one year, 11% for three years and 2.8% for five years. The long term survival for those without nodal involvement was 50% for one year, 25% for three years and 14% for five years.

Recently T. Peterson, F. Johnson[309] and Kiser reported a local series of thirty patients with carcinoma of the esophagus or high gastric carcinoma upon whom resection of the tumor was carried out from 1956 to 1966 with reconstruction by esophagogastric anastomosis in the pleural cavity. There were four postoperative deaths, 13%, three late hospital deaths, 10%. Eleven were alive without evidence of tumor, four for over five years. Eleven (36%) died from metatases within eleven months.

The recent report by Fry,[117] Grein and Adams of Chicago on carcinoma of the upper esophagus with malignant tracheo-esophageal fistula treated by radiation followed by surgical excision with no recurrence four years later is encouraging and might give rise to the hope that with combined therapy a less pessimistic attitude might be justified. A review of the whole picture with all factors evaluated indicate that carcinoma of the esophagus presents a less dismal outlook now than previously. Certain facts stand out. The stomach is not the ideal substitute for the esophagus following resection. The right colon is available and retains its blood supply better than the jejunum and can be used more safely. Irradiation has been a factor in prolonging survival time with and without other treatment, and its use is to be encouraged. Earlier diagnosis and an aggressive attitude towards epidermoid carcinoma by surgery and irradiation has considerable to offer for this otherwise hopeless condition.

Pericarditis and Constrictive Pericarditis

Disease of the pericardium apparently was recognized long before anything was done about it. Roilan[341] in 1649 suggested incision and drainage of the pericardium through a trephine opening in the sternum. Senac in 1749 suggested drainage through an incision to the left of the sternum. Romero[343] in 1819 apparently did the first successful pericardiotomy recording two recoveries in three cases. Jowett[193] in 1827 did a transpleural trocar drainage allowing the fluid to escape into the pleura from which it was absorbed. Karanoff[198] in Russia in 1841 successfully drained a series of patients with effusions from scurvy (bloody effusions?). Hilsman[173] in 1844 was the first to drain suppurative pericarditis through a left fourth interspace incision. Langenbeck[229] did the same in 1850.

Del Vecchio[79] in 1895 demonstrated in dogs that heart wounds heal following suture. Fischer[108] collected 452 cases all but 72 fatal. Tuffier in 1920 collected 305 cases from which 50% recovered. The status of such procedures at that time was expressed by Billroth's[29] description, "A Surgical Frivolity. No surgeon who wished to preserve the respect of his colleagues would ever attempt to suture a wound of the heart."

Beck[21] in 1925 noted several points. Blood in the pericardium absorbed rapidly and left no adhesions. Tamponade occurred from very rapid formation of fluid and not from slow formation. Drainage was not desirable except to the pleura.

Delorme[80] in 1898 suggested decortication be done for constrictive pericarditis the same as in the trapped lung but it was not carried out. Brauer[40] in 1902 resected the overlying ribs and cartilages in an attempt to relieve the situation. The patient was well eleven years later. Rehn[325] in 1914 was the first to report the results of partial pericardiectomy.

Sauerbruch[355] reported one case done in 1913. Churchill[55] in 1929 reported the case of an 18-year-old girl operated upon in July, 1928, resecting five cartilages and the left half of the sternum decorticating an area the size of the hand freeing the auricle and elevating the heart. He collected 37 cases with seven deaths and 50% excellent results. Harrington[160] in 1940 reported on nine cases with three cured, three improved and three deaths from 1936-1939. Later in 1944,[162] the series was up to 44 cases with a 25% mortality, three cases were tuberculous. Claude Beck[24] in discussion reported on 51 operations on 46 patients with 67.4% cure. There were 26% early and late deaths. George J. Heuer[170] reported 14 of 18 patients cured or markedly improved. Wangensteen[419] in 1932 reported on his first three pericardiectomies. Clagett, Kirklin and Cooley[63] in 1958 reported on the entire Mayo Clinic series of 72 patients from 1935-1955 with essentially complete removal of the peel in 65 cases. Eleven of the patients showed granulomatous changes suggestive of tuberculosis of whom six had positive cultures. Stanley Maxeiner[262] and this author independently carried out a small series of this type of surgery in the private hospitals in the early forties.

Josiah Fuller[118] of Duluth carried out the first pericardiectomy at the Head of the Lakes in 1957.

Patent Ductus

Persistent Ductus Arteriosus was recognized by Galen A. D. 131. Botallo, due to a mistranslation by Van Horne in 1660, has been credited with recognizing the condition and his name given to it (Ductus Botalli) but he has no claim to it. Harvey in 1628 recognized the purpose of the Ductus. Gibson[128] in 1898 described the murmur associated with it. Seammon and Edgar Norris[350] reported on the time of closure of the ductus and inter auricular septum in 1918. John C. Munro[282] in 1907 suggested and described a technique for ligation but never performed it. When Dr. Elliot Cutler[72] was in Minneapolis to give the Dr. E. Starr Judd lecture, "Total Thyroidectomy for Cardiac Disease," at the University of Minnesota in February, 1937, he was asked by George Farr and Arthur C. Kerkhof to see a woman who had a persistent ductus and decide if there was not something to be done for the condition. He said "not at this time, but send her down and we will see if something may not be done." The patient, a young woman, refused to go to Boston and nothing was done. John W. Strieder,[143] Graybeil and Boyer in 1937, attempted to ligate a ductus unsuccessfully, the patient dying on the fourth day with the ductus still patent. Robert Gross[146] and Hubbard of Boston carried out the world's first successful ligation in 1938. J. Jones, S. Dolley and Lewis Bulloch[190] in 1939-40 reported on a series. Jones[190] stated that for a full year before Gross' first case he had been trying to obtain permission to operate upon such a patient without success. Bruns and Stephen attempted to ligate a ductus but ligated only some fibrous tissue. Tourof and Vessell in 1940 successfully ligated the ductus in a patient with bacterial endocarditis. Clarence Crafoord[66] performed his first ligation of patent ductus in 1942. M. Shapiro[368] and Ancel Keys of Minneapolis in 1943 reviewed the course of patients with an unoperated ductus arteriosus and the prognosis from it. Clagett, Kirklin, Ellis and Cody[59] reported upon 223 patients operated upon at the Mayo Clinic between January 1, 1940 and December 31, 1953. Krovetz and Warden[221] in 1958 reported on 515 cases from the University of Minnesota Hospital from 1939-1958.

On the Minnesota scene the first patent ductus operation apparently was done by Wangensteen[420] in 1939 and with Varco and Baranofsky reported on 76 cases emphasizing the importance of divi-

sion of the duct over ligation. The first operation at the Mayo Clinic was in 1940.

From the local private hospitals I did my first patent ductus operation at Swedish Hospital[207] in 1943, ligating the ductus in a young woman with bacterial endocarditis, left pleural effusion, three pulmonary infarcts and positive blood culture. She recovered with only a little sulfa drug and is alive and healthy to date. We continued to do a considerable volume of this work for Shapiro and others in Minneapolis General Hospital, St. Mary's, Abbott, and Northwestern Hospitals, until September, 1946, when Tague Chisholm[54] joined O. S. Wyatt in pediatric surgery. He had been trained in cardiovascular surgery by Robert Gross in Boston. Working together for a number of years, this work continued in various hospitals doing coarctations, Blalocks, et cetera, and in 1947, a division of a double aortic arch at Abbott Hospital.[208] This was believed to be the first in the state. The first operation for patent ductus arteriosus at the Head of the Lakes was done by Josiah Fuller[118] in 1953. Subsequently Jensen, Schmidt et al.[185] continued this type of work in Minneapolis, then going on to other cardiac surgery.

Coronary Artery Disease

Beck[23] of Cleveland was the first to attempt to obtain additional blood supply to the myocardium damaged by coronary disease creating adhesions to the pericardium by abrasion, by talc insufflation and later in 1935[22] by suture of a pedicle pectoral muscle flap onto the myocardium. L. O'Shaughnessy[298] of England in 1936 used a pedicle of omentum brought up through the diaphragm as a better vascular supply. Lenzius[236] in 1937 excised the pericardium and attached the lung to the myocardium. Fauteux[105] in 1940 ligated the vena magna cordis with the same idea in mind. Arthur Vineberg[407] of Montreal beginning in 1946 and in a continuing series of studies and reports has been a staunch supporter of internal mammary transplants to the myocardium to create additional blood supply to the injured myocardium and has demonstrated persisting anastomotic channels by injection techniques. Many modifications have followed. Some surgical groups have become enthusiastic, others disappointed. Ripstein[329] in 1948 stated that there was no lasting benefit from all types of procedures. An editorial[93] in the *New England Journal of Medicine* in August, 1966, was skeptical. Relief of anginal pain has been recorded frequently. On the local scene Baranofsky[17] and Sparafka from Ancker Hospital in 1954 used defunctionalized jejunal transplants to add blood supply. Ferlic,[107] Quattlebaum and C. Walton Lillehei in 1966 used an arterialized vein graft from the left subclavian artery for this purpose.

Vineberg[408] more recently added another technique involving the removal of the epicardium and the covering of the adjacent aorta, then wrapping the heart with a free omental graft. Sufficient time has not elapsed to evaluate this procedure. Recently another suggestion for increasing myocardial blood supply by multiple ventricular puncture through the damaged area with a #19 needle to encourage new vascular channels has been reported by Khazei et al.[202] and Sen et al. Pifarre[313] et al. in September 1969 deny any clinical or experimental evidence to support its use.

The recent article by Bloomer et al.[34] on the use of the splenic artery for myocardial revascularization is worthy of note.

An analysis of the effects of mammary implantation by Mantini,[259] Tanaka and Lillehei has recently appeared. The recent favorable report of Urschel,[403] Paulson et al. and their discussants on the use of "Aorta to Coronary Artery Vein Bypass Grafts for Coronary Artery Occlusive Diseases" will be followed with great interest.

Cardiac Surgery

Mitral Stenosis

Mitral stenosis, that crippler and killer of young people, had long resisted all efforts at medical treatment. Could surgery do any better? Cushing, Carrel[51] and others had tried experimentally to produce and surgically relieve cardiac valve lesions without too much success. Elliott Cutler[71] of Boston in 1923 using a cardiovalvulotome incised a stenotic valve in a four and one-half year old girl who survived, living four and one-half years before dying from progressive heart disease. This patient, however, was the only survivor of six so treated.

Duff Allen[6] and Evarts Graham of St. Louis in 1923, through a ventricular approach with their cardioscope, attempted to cut the mitral valve but the patient died on the table under anesthesia. Souttar[378] of England in 1925 dilated a mitral valve with his finger introduced through the left

atrial appendage for the second successful case. Charles Bailey[15] on November 14, 1945, using a hooded knife along his finger through the auricular appendage, incised a stenotic valve but the patient died of hemorrhage. After three more failures on June 10, 1948 he successfully incised the commissure in a 24-year-old woman who survived. After failing with a valvulotome in 1947, Dwight Harken[152] of Boston on June 16, 1948 successfully excised a portion of the anterior commissure. By 1950 he had two successes in five attempts. He came to favor finger fracture while Bailey favored the knife. Brock of England[42] successfully used finger fracture and by 1951 had done 47 cases, losing seven of the first twenty. Charles Dubost[90] of Paris in 1953 used a transatrial dilator successfully and by 1962 reported a 2% mortality in 965 valvulotomics. Andrew Logan[251] of Edinburgh used a trans-ventricular mechanical dilator in 1955 with success.

The first successful open operation for acquired mitral disease in the world was done in 1956 by C. Walton Lillehei[244] at the University of Minnesota Hospital. A similar operation was done later that year by K. A. Merendino,[272] formerly of the University of Minnesota, now at the University of Washington.

V. L. Gott[135] inserted the first successful prosthesis for mitral insufficiency at the University in 1957. Starr[383] in 1961 introduced the ball valve prosthesis with six survivors in eight patients. The Starr-Edwards modification followed and later valves by Barnard, Hufnagle, Conrad, Alvarez, Diaz, Cross, Jones and Kay. Aortic homografts were also used. The first closed mitral commissurotomy at the Mayo Clinic was done in 1951.[99] Their first open heart operation on the mitral valve was carried out in 1955. The first valve replacement was done in 1960. Few were done to 1962.

A complete record of the Mayo Clinic experience with surgery for mitral disease by the team of Kirklin, Ellis, McGoon and Wallace has appeared in Ellis' excellent book, "Surgery for Acquired Mitral Valve Disease,"[99] published in 1967.

Heart Pump

The idea of a mechanical heart pump is far from new. Dale and Schuster[73] of London in 1928 constructed a machine to pump the blood but provided no mechanism to provide oxygenation or carbon dioxide removal. Jongbloed[192] in 1948 produced a machine for both circulation and oxygenation of the blood but did not use it. Melrose[270] of London in 1949 started a machine but did not complete it until 1957. Gibbon,[127] Miller and Fineberg through International Business Machine in 1949 produced a complete machine and with it in May, 1953, were credited with the first successful open heart operation, repairing an interatrial septal defect.[127]

Dennis and Varco are reported to have done the first open heart operation with cardiopulmonary bypass in 1950. F. John Lewis and Varco[404] did their first open heart operation under profound hypothermia in 1952. Dennis[82] and Varco on April 5, 1951 attempted to close an interventricular septal defect by open operation with a pump oxygenator but the patient succumbed on the table. The first successful open heart closure of an interventricular septal defect under cross circulation was carried out on a ten-month-old infant on March 26, 1954 by Lillehei,[243] Varco, Warden and Cohen. Lillehei[243] on September 1, 1954 did the world's first complete repair of the Tetrology of Fallot under human cross circulation. He had on August 6, 1954 carried out the world's first repair of an atrioventricular canal under cross circulation. Lillehei and Varco on May 13, 1955 did the first successful closure of an interventricular septal defect under cardiopulmonary bypass using a bubble oxygenator. Lillehei on January 30, 1957 placed the first myocardial electrode for complete heart block. He later on October 31, 1958 did the first prosthetic aortic cusp replacement for aortic stenosis.

F. D.. Dodrill[86] of Detroit with the help of General Motors engineers in 1953 produced a very efficient pump which would by-pass one-half of the circulation. The Swedish team of Bjork[31] and Crafoord on March 20, 1953 using a pump oxygenator performed the second successful open heart procedure. John Kirklin et al. of the Mayo Clinic, using the improved Mayo Clinic model of the Gibbon-IBM machine, successfully closed a septal defect for the third such case in a five and a half hour operation with 40 minutes of open heart surgery.

E. Dennis[82] et al. in the spring of 1951 developed a simple and cheap heart pump which they

subsequently used. Following the suggestion of Morley Cohen,[243] Gilbert S. Campbell[244] carried out on over a hundred dogs the technique of using another animal lung to oxygenate the blood (cross circulation) and found it feasible. Drs. Varco and C. W. Lillehei[222] on March 23, 1955 successfully operated upon a 13-year-old boy, closing three traumatic holes in the heart using a dog's lung for an oxygenator.

For a time the University Hospital used human beings for cross circulation but this was discontinued as pump oxygenators were improved and became available. By January , 1956, 97 patients had been operated on at the[376] University of Minnesota Hospital and 38 at the Mayo Clinic. The work continues at an accelerated pace.

Cardiac Surgery in Minnesota

Cardiac surgery apparently was initiated in Minnesota by Drs. F. C. Mann,[258] J. Priestley, Markowitz and Yater in 1930 with "Transplantation of the Intact Mammalian Heart" the report of a series of homotransplants to the cervical region of dogs, presented to the Mayo Clinic Staff Meeting of April 22, 1931.

Thoracic Surgery which at first developed slowly from crude beginnings has in recent years blossomed suddenly along some lines. The most spectacular has been in the field of open heart operations and organ transplants. The extensive experimental laboratories of the University of Minnesota, the Mayo Clinic Institute and later the U. S. Veterans Facility have developed a large number of individuals, techniques and procedures which have made many of these operations possible. From the faculties and graduates of these facilities have come a number of the outstanding cardiovascular surgeons of the world. Among those who have been exported to top positions around this country and the world have been: John W. Kirklin, C. Walton Lillehei, Alvin Merendino, Clarence Dennis, Bernard Zimmerman, John Paine, F. John Lewis, Morley Cohen, Ivan Baranofsky, Herbert E. Warden, Richard Dewall, Vincent Gott, Fletcher Miller and others. It is worthy of note that Christian Barnard, Norman Shumway, C. Walton Lillehei, C. Cabrol and D. Lepley were trained at the University of Minnesota. A number of Dr. E. Zebrini's associates were also Minnesota-trained.

Thoracic surgery, more particularly the cardiac and transplant type, have ceased to be a lone surgeon's job. It has become a team effort not only from the diagnostic standpoint but very much so from the surgical. The original teams for open heart surgery involved at least fifteen individuals and two or three cases per week were maximum, even in the large surgical clinics. Now with smaller teams involved, it is not unusual to have several cases scheduled per day. The transplant procedures require even larger groups. A recent multiple transplant of heart, lung and both kidneys by DeBakey et al. at Houston involved some 70 members of the operating teams.

Cardiac surgery was introduced to St. Paul at Ancker Hospital by Merendino and Baranofsky who carried on this work from 1949-54. Later Baranofsky started transauricular procedures for mitral stenosis and transventricular operations for aortic stenosis. Coarctation and Blalock operations followed. At the private hospitals, Sam Hunter[179] did his first mitral surgery at Miller Hospital in 1954 and implanted a pacemaker in 1959 at Bethesda. His first open heart surgery for a septal defect was in 1958 at St. Joseph's where he later did valve replacements. The same type of procedures were carried out at Miller in 1960. Cardiovascular surgery has been continued since that time at both places.

The team of Connolly, Culligan and Gannon also have continued vascular and cardiac surgery experimentally and clinically.

Josiah Fuller, a Rochester-trained thoracic surgeon, arrived in Duluth in 1953, where he has done thoracic and vascular surgery since that time. He did his first Patent Ductus May 23, 1953 at St. Mary's Hospital, Duluth, Mitral Commissurotomy March 23, 1954, Congenital Vascular ring May 3, 1956, Pericardiotomy February 26, 1957 and Coarctation July 3, 1957.[118]

Cardiac Transplants

The first human heart transplant in the world was performed on December 3, 1967 at Groote Schuur Hospital in Cape Town, South Africa, by Dr. Christian Barnard et al. on a 53-year-old man, Louis Washkansky, who *died* on December 21 of pneumonia. A team of 29 was used.

By late September, 1968, more than 50 cardiac transplants had been carried out in various clinics throughout the world. The short term mortality in this group of approximately 25 brings the

total mortality for the entire series to near 50%.

The number of transplants increased so rapidly that by December, 1968, over 100 had been reported, and by February, 1969, 114. Additional countries entered the race with operations reported from the Soviet Union, Turkey, Japan, Israel, Poland and West Germany. Additional cities have also been added on this continent with Toronto in Canada, Richmond, Virginia, Chicago, Milwaukee, Cincinnati, Denver and Ann Arbor.

Like most innovations, the advent of cardiac transplantation late in 1967 has added social, moral, ethical, legal and financial and other problems to the medical-hospital scene.

Lung Transplants

Much experimentation has been done on the problem of tissue and organ transplantation. Blood was the first to be used successfully after the problem of matching and agglutination was solved. Bone preserved or of foreign sources, while it did not survive, did remain as a scaffold until new growth took over. Corneal grafts were successful replacing scars and opacities. Skin grafts persisted long enough in burns for emergency use as a temporary covering. Kidney transplants between identical twins were made with a high degree of success. Later when made between close relatives a fair degree of success was accomplished. Intensive studies of rejection phenomena and immune suppressive drugs have increased the chances of success in this field.

The transplantation of the lung has presented problems from the start. Carrel and Guthrie[50] in 1907 were the first to transplant the lung, moving both lungs, the aorta and vena cava from a one-week-old cat to the neck of a large cat. This was not a sterile transfer but the lungs survived for 48 hours uutil infection developed. Dimikhof[81] in 1947 carried out homografts of individual lobes. Staudacher, Bellinazzo and Pulin[382] of Italy did auto and homotransplants of the right lower lobe in dogs. The auto transplants maintained function and anatomical integrity for 12 days. The homotransplants were rejected in eight days. From 1951 to 1956 Lanari, Croxatto and Molin carried out extensive studies with similar results. The first successful autogenous transplant of lungs in animals with long survival was reported by Juvenelle,[195] Citret, Wiles and Stewart in 1951. Portin,[317] Rasmussen, Stewart and Anderson reported followup in 1960. Sim, Yacoubain,[375] Summonian and Sahyoun from the American University of Bierut in 1965 reported one dog surviving 22 months after a staged bilateral reimplantation of the lungs. The ventilatory response to exercise and hypercapnia was essentially normal. Steady improvement of cardiopulmonary function was noted. There was no evidence of vagus nerve regeneration. The animals did not show the pattern of denervated breathing. There was uneven ventilation and persistent hypoxemia at rest. At necropsy there was slight thickening of the alveolar walls.

Studies by Nigro,[290] Reiman, Mork, Frey, Benfield and Wm. E. Adams of Chicago in 1963 on dogs surviving with a reimplanted lung, two of whom survived over one and a half years, by bronchospirometric and pulmonary artery pressure readings showed pulmonary ventilation was only slightly depressed but oxygen uptake was significantly decreased and pulmonary hypertension developed in all animals even with no anastomotic stenosis. The Surgical Forum #XVII[339] of the 52nd Clinical Congress of the American College of Surgeons in 1966 had several reports on various phases of lung transplant. Secrist[366] and Trummer in 1967, testing for Herring Breuer reflex after reimplant of lung, reports that six of 14 dogs showed evidence of some return in seven months while the rest showed none in four to 54 months, suggesting some regeneration of afferent vagal limb. Necrosis of the bronchial suture line and stenosis of the vascular anastomosis occurred not infrequently.

To date, five transplants in humans have been carried out.

Moore et al. have compiled a list of the five total lung transplants, three from the United States and one each from Scotland and Canada. All succumbed in from seven to 28 days. One lobe transplant from Japan had to be removed 18 days later.

The most recent lung transplant patient operated upon at the University of Michigan on September 1, 1969 died on September 4, 1969.

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I have also drawn freely on my memory of many of the events recorded and my personal acquaintence with many of the individuals mentioned.

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Minnesota Medicine

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Section 2 of Two Sections

Improving Health Care in Minnesota

Reports From

Northlands Regional Medical Program, Inc.

MINNESOTA MEDICINE
Volume 55, December, 1972, Supplement No. 3



Mary Jane Ryan BS, MS, PhD

August 5, 1914—September 7, 1972

Northlands Regional Medical Programs has lost a leader with the death of Dr. Mary Jane Ryan. No person in Minnesota has been more dedicated to the purpose of making scientific information available and accessible to improve medical care.

Her role as Liaison Librarian for NRMP, stimulated Biomedical Libraries in Minnesota to develop an efficient Library System. It is fitting to dedicate this supplement of MINNESOTA MEDICINE to Dr. Ryan in memory of her accomplishments in biomedical library science.

With dedication she supported innovative educational programs and provided leadership in making available the latest biomedical information. She gave freely of her time and talents and stimulated others to do likewise. Her article in this series documents many of her recent accomplishments.

Dr. Ryan was an enthusiastic example of the concept of lifetime learning. After graduating from the College of St. Catherine in 1937 she returned repeatedly to educational institutions to improve her knowledge. She was granted an MS degree from the University of Southern California in 1955 and a PhD in Educational Psychology from the same institution in 1967. During her career she served in ten different educational institutions in South Dakota, New York, California, Wisconsin and Minnesota.

The quantity of her life was not great, but the quality will live on as a memorable inspiration for those of us who knew her so well.

Winston R. Miller, M.D.
Director
Northlands Regional Medical Programs

This publication is dedicated to the memory of Mary Jane Ryan, PhD, Liaison Librarian of NRMP, who passed away on September 7, 1972

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A Five-Year Perspective of NRMP

WINSTON R. MILLER, M.D.

Like society as a whole, the health care system is changing. NRMP acts to stimulate these changes in a positive way. Of necessity, the program itself has also changed. Continuing effectiveness in an RMP requires inherent flexibility—the capacity to change and influence change in new ways as new and important issues come into prominence.

The Categorical Disease Phase

Evolving from President Johnson's National Commission Report entitled "A National Program to Conquer Heart Disease, Cancer and Sroke," initial emphasis was on the three categories of disease which cause seventy percent of all deaths. Although the program stirred up controversy, the almost altruistic principles in the RMP law were virtually irrefutable: making the latest scientific advances available to all people; improved cooperative arrangements among all providers of health care services; local authority and administration; a federal-private partnership; no interference with existing methods of practice or payment; incentive awards to stimulate improvement; and improved continuing education for health care professionals. The emphasis on the principal causes of death and disability repeated the time-honored concern of all human societies.

In 1965 a social revolution in America had already started; the accepted socio-political proclamation of "Optimum Health Care as a Human Right" propelled the health care system into the forefront of the social change process. The significance can hardly be overemphasized. The Declaration of Independence proclaiming "life, liberty and the pursuit of happiness" as fundamental human rights has dominated our society since its adoption. Adding optimum health care to this social premise virtually forces major social revisions.

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The new system of Regional Medical Programs created high hopes for rapid accomplishment. In fact, the lack of rapidly accelerating momentum nearly caused its demise in 1970 and 1971. Since mid-1971 accomplishments have increased significantly, and this unique federal-private partnership organization has received wide recognition.

Like most RMP's, NRMP started with categorical emphasis, and placed priorities on continuing educational programs for providers of health care services.[1] Although controversy existed as to who would get how much money to do what, the goal of the program was fairly simple. It was to develop optimum health care for patients with categorical diseases, utilizing mechanisms involving new cooperative arrangements and new programs of continuing education.

Change to Broader Goals

The categorical disease focus was short-lived. In less than two years the leaders of NRMP recognized that this new program was really directed at change in the health care system as a whole. Any program which would have a significant effect on the diseases which cause seventy percent of all deaths must address itself to problems in three broad areas of concern: (1) How to produce more effective programs of continuing and patient education; (2) How to correct the shortage and maldistribution of health manpower; (3) How to develop more effective delivery of health care services.

In November, 1968, the Board of Trustees adopted the broad goal of equal and optimum health care services for all of the people in Minnesota. The program staff was directed to conduct or get others to conduct studies to provide better definition of the many unmet needs. Incentive funding of demonstration projects was directed toward the "seed money concept" of stimulating constructive and long-lasting changes. Application of the principles of applied research changed program design from simple subsidization of good activities to prototype studies or demonstrations

for innovative improvements in the health care system.

Education, Manpower and Health Services Development Committees developed policy statements which outlined goals and objectives for the program. These three committees carried responsibilities in planning specific activities, reviewing all applications and management of funded studies and demonstration projects. The intent was to develop a mechanism whereby all activities would fit together in a rationally organized system and respond to specific goals and policies. This philosophy has influenced all planning studies, feasibility studies and demonstration projects.

The change in program design away from the categorical emphasis caused some chagrin among personnel and institutions specializing in categorical diseases. However those working on categorical staff or project activities continued and completed their commitments, while new activities were being undertaken with broader horizons. The planning and feasibility studies conducted by the NRMP staff are shown in Table 1. Table 2 lists all extramural projects conducted between 1968 and 1971. The articles in this supplement of MINNESOTA MEDICINE include reports on seven projects which have now been completed or nearly completed.

TABLE 1
Planning and Feasibility Studies by NRMP Staff

I. Education

Title	Authors	Date
*Patterns of Continuing Medical Education Among Minnesota Physicians	Fahs and Miller	Oct., 1968
*Evaluation of the ETV Program "Monday for Medicine"[5]	Fahs and Miller	July, 1968
Health Manpower Distribution[6,7,8,9]	Fahs and others	1967-1968
*Continuing Education in the Health Professions: An Annotated Bibliography	Leyasmeyer and Whitmarsh	1969
Continuing Education Resources in Nursing	Schowalter	1972
Nursing Audit in Hospital Nursing	Schowalter	1972
†A Statewide System of Continuing Medical Education Based on Medical Audit[2]	Fifer and Schless	1970-1972
*An Appraisal of the Dial Access Medical Library	Berglund, Hill and Miller	1969
†Development of a Medical Library Network[3]	Ryan	1972
Medical Library Service for Minnesota[4]	Foreman and Lorrig	March, 1971
Library Services to Community Hospitals	Ryan	1971
*Recommended Textbooks for a Core Medical Library	Ryan	1971
*Exchange: Fruit Fix-Ups	Verstraete	1971

II. Health Manpower

Title	Authors	Date
*The Changing Dimension of Physician Manpower	Hill, Miller and Sonderegger	1970
*Physician Manpower Inventory	Hill and Campbell	1970-1972
*Physician Manpower Needs of Medical Groups	Hill and Miller	1971
*Physician Migration	Cole, Sonderegger and Miller	1971
Relationship between Place of Internship and Residency to Location of Practice	Hill and Campbell	1972
Public Perceptions: Physician Assistants	Litman	1971
*The Office Trained Dental Assistant Program	Place, Hill and Campbell	1971
*Nursepower in Minnesota	Cole and Schowalter	1971
Industrial and Office Nursing	Schowalter	1972
*Allied Health Manpower Statistics	Deschler and Schaefer	1969
Roles of Physical Therapists	Deschler	1972

III. Health Services Development

Title	Authors	Date
*Profiles of Regional Health Variables	Cole, Miller and Simons	1969
*Regional Health Variables	Hill and Arndt	1972
*Parameters of Medical Practice	Miller, Cole and Simons	1969
*Freeborn-Mower County Health Services Regionalization	Dornblaser and Wilkins	1970

*Final reports have been published by NRMP.
†See reports in this supplement of MINNESOTA MEDICINE.

TABLE 1 (continued)

III. Health Services Development

Title	Authors	Date
*Regional Cooperation: A Design for Sharing Among Health Care Institutions	Metcalfe	1971
*Attitudes of Small Hospitals Toward Regional Cooperative Arrangements	Chowins	1971
*Minnesota Health Care Opinion Survey	NRMP, Blue Cross, CHP	1971
*Utilization and Patient Origin in General Acute Hospitals	Arndt and Hill	1972
Evaluation of Mobile Health Unit: Southeastern Minnesota Community Action Council	Hill and Campbell	1972
Evaluation of Plainview Rural Health Care Facility	Evans, Carter, Nobrega and Reilly	1972
Health Care Needs of Metropolitan Black Minority	Hill, Arndt and Campbell	1972
Rehabilitation Needs and Resources in Rural Areas	Deschler	1972
*Cancer Mortality Rates: 25 Years	Hill, Berglund, Cole and Miller	1971
*12 Year Review of Cancer Mortality	Berglund and Hill	1972
*A Profile of Radiation Therapy	Berglund, Hill and Miller	1970
Dental Resources	Place	1972
Utilization Review in Rehabilitation Facilities	Deschler	1972
Communication Methods of Voluntary Health Agencies	Kiley	1972
The Profile of Medical Practice	Hill, Campbell and Miller	1972

*Final reports have been published by NRMP.

TABLE 2
Extramural Projects—1968-1971
I. Planning Projects

Title	Sponsoring Organization	Duration of Project
A State-wide Program for Intensive Coronary Care Units	Minn. Heart Assoc.	1968
Rural Health Care Study	Univ. of Minnesota	1968
Postgraduate Education in Pediatric Cardiology	Univ. of Minnesota	1968
Regional Program for Pediatric Solid Tumors	St. Louis Park Med. Center	1968
Renal Dialysis Training for Physicians	Mayo Clinic	1968
Standards of Medical Practice	Minn. State Med. Assoc.	1970

II. Operational Projects

Title	Sponsoring Organization	Duration of Project
Heart, Cancer and Stroke Project	St. Paul Bureau of Health	1968
*Improved Care for Myocardial Infarction	Minn. Heart Assoc.	1969-1971
*Postgraduate Education in Pediatric Cardiology	Univ. of Minnesota	1969-1971
*Diabetes Regional Center Education	Diabetes Education Center	1969-1971
*Stroke Education	Amer. Rehab. Foundation	1969-1971
Dial Access Medical Library	NRMP Staff	1969-1974
Intensive Coronary Care Training for Nurses	Minn. Heart Assoc.	1970-1971
*Refresher and Continuing Nurse Education	Minn. Jr. College System	1970-1973
*Continuing Education for Laboratory Personnel	Minn. Soc. of Med. Technol.	1970-1971
*Education in Clinical Nutrition	Diabetes Education Center	1970-1971
Short-term Residencies in Medicine	Mayo Clinic	1970-1971
Mobile Health Care Unit	Polk County Nursing Service	1971-1974

*See reports in this supplement of MINNESOTA MEDICINE.

Change to a More Structured Approach

In 1971 NRMP embarked on a new methodology of program design. It consisted of two components: (1) detailed job descriptions and planned activities for all members of the employed staff, (2) specific contract offerings for all extramural project applications.

Deriving the basic idea from informal discussions at national meetings, NRMP pioneered in extensive development of the method. Successful implementation evolved from several facts and convictions:

1. Specific planning would facilitate a more structured and integrated program.
2. Committees of the Regional Advisory Group had developed a clearer sense of direction for priority needs.
3. Management of contracts could be more structured than management of project grants, making coordination and performance responsibility more rational and acceptable.
4. The principal areas of need lay in improved primary and secondary health care services, and the "experts" in these spheres were more often outside than inside the medical centers.
5. Small contract offerings would facilitate participation by many more institutions, thus increasing program involvement.
6. Anticipated funding was limited, and more activities could be supported with specific offerings and small total budgets.
7. Regional Medical Programs had gained momentum slowly, and short-term accomplishments were needed.
8. Smaller institutions could handle small projects better than large ones, and might be expected to contribute proportionately more of their own resources.

Program Staff Activities

Job specifications for the 16.4 (full-time equivalent) members of the professional staff and 12.7 members of the secretarial and clerical staff were divided into six subdivisions: (1) Program direction and administration; (2) Project development, review and management; (3) Professional consultation, community relations and liaison; (4) Planning studies and inventories; (5) Feasibility studies; (6) Central regional services.

In 1972, program direction and administration consumes eight percent of the budget, while consultation, community relations and liaison activities use 7.4 percent. Professional staff personnel are directed to help to strengthen cooperative programs among health care personnel and institutions throughout the state. In the past year they traveled over 100,000 miles within the state carrying out their multiple responsibilities.

Planning and Feasibility studies consume 18 percent of the current budget. These studies document unmet needs, analyze attitudes toward proposed constructive changes, inventory resources, introduce innovations, and stimulate regional and subregional network development. The final reports of these studies are circulated widely throughout the state in a deliberate attempt to produce maximum impact. Many of these studies have been completed; some have been published in the medical literature,[2-9] and some are still in process. Although NRMP cannot document the impact of planning and feasibility studies quantitatively, many of the benefits are known. Health planning endeavors throughout the state have used these reports as background resources for their efforts; the legislature has used the contained information for passage of new legislation; many organizations have used the information for development of innovative health care programs; and many of the reports have been accepted as the latest and best information available.

Communication and public relations activities have helped to promote widespread understanding and appreciation of the need for stronger cooperative linkages. The regionalization movement has been publicized by a newsletter, "Northlands News" to a mailing list of 11,000; newspaper articles totaling 4000 inches in 1971; exhibits at all major meetings of health-related organizations; and speeches by professional staff members at many local and national meetings.

The need for an unbiased, multidisciplinary staff of "experts" in the health care field has been reinforced lately by fulfillment of five outside requests for specific evaluation and development studies. One of these, supported by a grant from the Hill Family Foundation, developed consensus recommendations for new experimental projects to improve the delivery of health care services to isolated Indian and white communities in the sparsely settled areas of northern Minnesota. The problem of optimum services for these isolated

communities is complex and difficult, but Minnesota has resources which should be able to grapple with such challenges.

Specific Contract or Project Offerings

Abstracts of 29 specific contract offerings were widely circulated in 1971 to solicit extramural activities which would conform to priority needs.

The activities proposed in the "Contract Offering Prospecti" were readily understood and accepted throughout the state. In the competitive review process, 43 applications from 28 different organizations were approved and ranked numerically in order of priority. Additional federal funding permitted activation of the 29 contracts listed in Table 3.

When it became known that 66 applications had been received in response to the contract offerings, other RMP's adopted the new method. Recognizing that the method represented a new research and development approach for RMP, the national RMPS office recently initiated a nationwide study to evaluate its relative advantages and disadvantages. Desirable attributes include a more structured program design, greater management potential, increased program flexibility, and more widespread involvement in the research and development effort.

NRMP is now conducting the review process for 1973 activities; 24 project offerings were circulated widely; and 69 applications were received

TABLE 3
Extramural Contracts—1972

I. Education

Title	Sponsoring Organization	Scheduled Completion
ICCU RN Education	Minn. Heart Assoc.	1974
Public and Patient Education	Comm. Univ. Health Care Ctr.	1973
Outpatient Medical Audit	St. Louis Park Med. Center	1973
Outpatient Medical Audit	Nicollet Clinic, Minneapolis	1973
Outpatient Medical Audit	East Range Clinic, Virginia	1973
Problem-oriented Medical Audit	Bethesda Luth. Hosp., St. Paul	1973
Problem-oriented Medical Audit	Charles T. Miller Hosp., St. Paul	1973
Coordinated Medical Information	Univ. of Minnesota	1973
Expand "RAISE"	Regional Approach to Improved Service Through Education, Wadena	1973
Dial Access Medical Information	NRMP	1974

II. Health Manpower

Title	Sponsoring Organization	Scheduled Completion
Physician's Assistant Education	St. Cloud State College	1973
Physician-Nurse Assistant	Mayo Clinic	1973
Nurse Associate in Adult Health	Univ. of Minnesota	1973
Nurse Associate in Gerontology	Univ. of Minnesota	1973
Innovations in Public Health Nursing	Minn. Dept. of Health	1973
Equivalency and Proficiency Testing in Nursing	Univ. of Minnesota	1973
Challenge Examinations in Nursing	College of St. Catherine	1973
RN for a Doctorless Town	Minn. Dept. of Health	1973
Operation MEDIHC	Minn. Health Careers Council	1973
Joint Recruitment of Physicians	S.W. Minn. Comm. Coop. Health Care Enterprise, Lamberton	1973
Nurse Refresher and Continuing Ed.	Minn. Jr. College System	1973

III. Health Services Development

Title	Sponsoring Organization	Scheduled Completion
Coronary Care Evaluation	Minn. Heart Assoc.	1974
Plan Areawide Coronary Care	Minn. Heart Assoc.	1975
Indian Health Care Services	Luth. Deaconess Hosp.	1973
Cervical Cancer Mortality Study	Univ. of Minnesota	1973
Hospital Staffing Methods	Minn. Hosp. Assoc.	1973
Rheumatic Fever Prevention	St. Paul Bureau of Health	1975
Model Health System	Univ. of Minn.-Lamberton	1973
Mobile Health Care Service	Polk Co. Pub. Health Nsg.	1974

by the July 17 deadline.

Developmental Fund Activities

A new opportunity was provided to NRMP with a "Developmental Fund Award" of $127,000 in 1972. This block-grant-type fund will support small short term studies and demonstrations during the fiscal year. The principle is to fund relatively small projects under the sole authority of the local review mechanism without the rather long delay period needed for the combined local and national review processes. The eleven developmental fund projects initiated as of this writing are shown in Table 4.

Network Development

Many program activities are directed at state or local network development. This kind of regionalization is based on the premise that cooperative networks offer the best solutions to some of the health care problems.

Medical Audit for Continuing Medical Education

A network of coordinated medical audit programs in community hospitals is being developed with cumulative participation of five additional hospitals each year.[2] Details of this activity are described by Dr. William R. Fifer* in a separate article in this series. The success of this program has attracted national recognition. Local medical leaders have been trained to lead their medical staffs in conducting medical audits of actual patient care performance. Continuing education programs are developed according to demonstrated needs, and follow-up audits determine improvement in performance. A new annual Minnesota Hospital Medical Staff Conference has been oversubscribed months ahead of time for the second consecutive year.

Regional Biomedical Library Network

With cooperation and assistance from the two medical center libraries, NRMP has led in development of a system making a full range of library information resources available and accessible throughout the state.[3,4] Details are presented by Dr. Mary Jane Ryan† in a separate article of this series. Components of this development include:

1. Loans of four sample core libraries to any health care institution in the state.
2. Workshops for library supervisors held in multiple areas.
3. Improved functional interrelationships with center libraries.
4. A reference book of all biomedical holdings at the two medical center libraries provided for all other libraries.
5. Library reference services as a part of the new toll-free Minnesota Medical Information Service Center.
6. Easy accessibility to the new national au-

*See page 17.
†See page 27.

TABLE 4
Developmental Fund Projects

Title	Sponsoring Organization	Project Director
Determination of Unmet Health Care Needs of Minorities and Low-Income Persons	Ramsey Action Programs, Inc.	M. E. Lundberg
Problem List and Multiple Variable Recording, Storage and Retrieval	Family Practice Dept., Univ. of Minn.	L. J. Filiatrault, M.D.
Oral Health Care Needs of Nursing Home Residents	St. Paul Dist. Dental Society	R. Wright, D.D.S. W. D. Ostergren, D.D.S.
Research to Improve Health Communications	Ramsey Action Program, Inc. & Dayton's Bluff Multi-Service Center	S. L. Brown
Consultation and Education in Nursing Homes	Minn. Nursing Home Assoc.	D. Layer
A Statewide Plan for Nursing Education	Minn. Higher Education Coordinating Committee	D. Draine, Ph.D.
Community Health Education Center (S.E. Minnesota)	Winona State College	D. L. Anderson, Ph.D.
Clinical Role: Community Pharmacist	Dept. of Clin. Pharm., Univ. of Minn.	H. F. Kabat, Ph.D.
Peer Resource Training	St. Paul-Ramsey Hosp.	J. Korlath
A Baccalaureate Program to Provide Career Mobility in Nursing	Univ. of Minn.	I. Harris, Ph.D.
Project Breakthrough Learning Center	Minn. Health Careers Council, Inc.	J. Koprowski

tomated literature search known as MEDLINE.

7. Assistance in obtaining National Library of Medicine grants to upgrade small biomedical libraries.

Rehabilitation Services

The development of a regional network for rehabilitation services promises to strengthen these services throughout the state. Studies of the distribution of services and facilities helped to document the need for network development, and the three rehabilitation centers at the Mayo Clinic, the Kenny Institute and the University have each developed new outreach relationships. Rehabilitation facilities in other parts of the state are also developing stronger linkages with peripheral institutions nearby. Several applications for the 1973 NRMP program seek to extend this network development.

Medical Center Outreach

NRMP has assisted or participated in development of several new outreach programs by Mayo Institutions: regional laboratory services; consultation services; rehabilitation services; short-term residencies; and a satellite clinic in a no-doctor town (The Plainview Health Care Facility).

At the University similar activities include new continuing education courses; consultation services; rehabilitation services; several programs for training new manpower disciplines; and Area Health Center development.

New outreach activities have recently been proposed from several secondary level medical centers—the St. Louis Park Medical Center, the Minneapolis Medical Center, the St. Cloud Hospital, and the Polinsky Rehabilitation Center in Duluth.

Area Health Education Systems

A recent supplemental award will enable NRMP to support and coordinate planning and development of eight community based Health Education Programs covering the state, with back-up support from the two medical centers. The purposes are: (1) Cooperative development of health manpower education programs geared to community needs; (2) Continuing education for health care personnel at the local level; (3) Patient and public education at the local level.

Emergency Medical Service System

Another supplemental award to NRMP will enable the Emergency Medical Services Unit of the State Department of Health to plan and develop a statewide system of comprehensive emergency medical care services. This system is intended to include: (1) Modern ambulances with well-trained attendants; (2) State-wide shortwave communications system; (3) Area and Regional Emergency Medical Care Centers staffed with specially trained personnel; (4) Emergency Medical Care Physicians with shortwave communication equipment.

End-Stage Kidney Disease System

National experts have publicized plans for multiple kidney disease networks in all parts of the country. As in many other fields, Minnesota has already made great progress in this development. Plans are now underway for expansion of this program to a multistate system which will provide optimum services for all patients in Minnesota, North Dakota and South Dakota.

Discussion

It has been difficult for many people to understand Regional Medical Programs—what they are, what their mission is, and how they try to accomplish their mission. Examples of difficult concepts are: federal-private partnership, catalytic activities to stimulate cooperative and construction change, regionalization and subregionalization, applied research and development, and health care systems development. The contract and project offering methodology has helped greatly to increase understanding.

NRMP provides funds for activities by many organizations, but it is not primarily a funding agency—all funded projects and contracts become integral components of the program, responding cooperatively toward broad regional goals. Although it does not support basic research, NRMP stimulates and supports applied research and development—the goal is improved delivery of health care *services*.

NRMP seeks to carry out its mission according to rational scientific principles. Rational solution for problems requires scientific analysis of needs, mobilization of resources necessary to meet those needs and demonstration projects providing convincing evidence of significant improvements.

It is of great importance that support be continued for unbiased research and development activities like those of RMP, to help insure maintenance of quality during this period of rapid changes in the health care system. The best talents in the country are needed to work on the problem

areas. They should not be thwarted in their efforts by any of the power blocks with vested interests (whether these be the federal government; syndicates of insurance companies, hospitals, health care corporations, medical centers or medical foundations; or the exclusive power actions of professional organizations). Applied research needs the same administrative milieu as fundamental research—one which permits a maximum of intellectual challenge, application of the scientific method, prestige and recognition rewards for accomplishment, and a minimum of rigid direction and management.

What is the future for RMP or RMP-like programs? In the immediate future RMP will probably play an increasing role in helping to maintain quality and develop new solutions to pressing problems. RMP is unique in that it has the potential for exerting considerable influence, without restrictive control by any level of government or by any of the power blocks in the health care system. It will be called upon increasingly to advance the science of applied research and development, to promote the fields of health care economics and health care systems development, and to use its multidiscipline staffs to provide evaluation studies and consultations for other organizations.

It seems probable that health care authorities or commissions will be developed to provide some kind of regulation of the health care industry. When this occurs, there will be jurisdictional changes in many publicly supported programs, and RMP will undoubtedly be one of them. Hopefully the desirable attributes described above will be preserved; it is believed that they will if our society continues to recognize the value of voluntary intellectual commitment and unbiased research and development.

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A System of Continuing Medical Education

Based on Medical Audit

WILLIAM R. FIFER, M.D.

THERE ARE 5,000 physicians in Minnesota who are in clinical practice. As individuals they are solely responsible for maintenance of their clinical competence. As student, intern or resident, the physician devoted all of his attention to learning. Now his principal activity is patient care. To do this job well, he must constantly update his medical knowledge. Due to rapid infusion of new information from biomedical research, a physician's knowledge store has a half life of less than ten years. A physician who fell asleep like Rip Van Winkle ten years ago would not know about Rhogam, about ethambutol, about staging procedures for Hodgkin's Disease, about coronary bypass surgery, about amniocentesis, etc. Regional Medical Programs were created to close the gap between the ivory tower and the practicing physician. Northland Regional Medical Program, like all Regional Medical Programs, has emphasized continuing medical education (CME) as the principal means to upgrade the quality of medical care. The basic question in CME is "Who needs to know what?" and we have begun to implement a statewide system of continuing medical education based on the determination of knowledge needs by review of actual patient care, medical audit.

Modes of Continuing Medical Education

How do physicians continue their medical education? First, patient care experiences are a vital learning resource. Second, consultations and daily contact with other physicians contribute greatly. Third, hospital staff meetings, medical and specialty society meetings provide new information. Fourth, continuation courses are provided in abundance. Fifth, reading medical books and journals continues to educate. Finally, innovative learning methods such as medical television, tape cassettes and videotapes are available.

Although there is no organization of this series of random experiences, there is certainly more continuing medical education offered than any of us can use.

Learning Theory

Educators tell us that retention of knowledge depends on its utility and its relevance.

Educators also tell us that there is a "teachable moment" at which time we are maximally receptive to new knowledge. In clinical medicine we reach the teachable moment when we are confronted with a clinical problem. We then call a consultant, go to the library, or in other ways acquire a *needed* piece of information to solve the problem of John Smith. We will remember the problem and our solution long after we have forgotten the source of our information.

Identification of Continuing Medical Education Needs

Given an almost unlimited number of opportunities to learn, how does a physician decide what to choose? When we divide medical practice into *what we know* (knowledge) and *what we do* (medical care), the question becomes: What is it we need to know in the context of what we do? There are three currently popular means of determining needs: *self-assessment tests, individual practice profiles, and medical audit.*

Self-assessment examinations are now offered by specialty societies in many fields. The internal medicine examination is called MKSAP-II, and is sponsored by the American College of Physicians. It is divided into nine subject areas and may be taken either as a closed or open book test. The examinee, after taking this test, learns two things: (1) what he *knows* of internal medicine divided into nine categories, and (2) how he compares with his peers.

Individual practice profiles measure not what a physician *knows* but what he *does*. Developed by

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the University of Wisconsin Medical School, this technique is as follows: A physician carries a tape recorder with him for several days, recording information for each hospital visit, office visit, and telephone call. The tape is then analyzed and a report describing his *practice profile* is sent to the physician. Along with the profile, the physician receives an educational prescription which says "inasmuch as you do *these things,* you need to *know* these things." The University then lists those courses, meetings, lectures, etc., most pertinent to the knowledge requirements defined by his practice analysis.

Medical Audit is defined as *a system of continuing medical education based on the evaluation of the quality of patient care as reflected in medical records.* We feel that medical audit is superior to either self-assessment exams or practice profiles in that it demonstrates the application of medical knowledge to patient care situations.

The Minnesota Medical Audit Program is funded by Northlands Regional Medical Program, and promoted by the University of Minnesota program staff. Described as a "Feasibility Study of Medical Audit," the program began April 1, 1971 in five Minnesota community hospitals (Austin, Fergus Falls, Hibbing, Virginia and Worthington). These hospitals were selected because of their diverse geographic distribution and because they were relatively "closed systems" in which the medical staff-hospital relationship was well established. Their sizes range from 64 to 185 beds, and their medical staffs contain from 17 to 40 physicians. Altogether, they comprise 142 physicians and 663 acute beds.

To qualify for participation in the study, we asked each hospital to meet four conditions: (1) approval of the program by the governing board, administration and medical staff, (2) medical records information retrieval capability (four of our first five hospitals have PAS/MAP), (3) willingness to create an education budget to respond to identified educational needs. and (4) apointment by the medical staff of one of its leaders to work 20 percent time as director of continuing medical education (DCME). Northlands Regional Medical Program provided the funds for the DCME position. It was understood by the hospitals that NRMP financial support would be withdrawn at the end of the one-year study period. We felt that one year was adequate to determine the value of the medical audit program in terms of improved patient care. Thus, we hoped to "set tops spinning" at a rate of five per year, and hoped they would keep on spinning after our seed money support was withdrawn. At present, four of the five will continue the program on their own, and we have begun working with four new hospitals. [Albert Lea, Fairview (downtown), Methodist (St. Louis Park) and St. Cloud] in the second year of the program which began April 1, 1972.

Methods

To implement our program, we have worked directly with the affiliated hospitals to assist their DCME's and medical staffs to establish a system of medical audit. In addition, we have conducted monthly medical audit workshops, an annual statewide hospital staff conference, and an annual continuation course on medical audit at the University of Minnesota. To establish an audit program in a hospital, we found it necessary to *teach the process* to the medical staff.

The *process of medical audit* involves six steps:

1. *Criteria must be defined* for optimum care of the disease or condition to be studied. If we study patients discharged with a primary diagnosis of diabetes mellitus, we set the recording of funduscopic examination for 95 percent of the patients examined as a criterion.

2. *Actual care must be reviewed* to display existing practice patterns. We may study 100 consecutive admissions for diabetes mellitus and find that 36 percent of the charts have funduscopic examinations recorded.

3. *Ideal vs. actual must be compared* to determine if a gap exists. In our example, the gap is between 36 percent actual performance and 95 percent optimal performance.

4. *Gaps must be translated into educational objectives* to form the basis for a continuing education program. In our example we state the objective in this way: "Following an education program on diabetic retinopathy, 95 percent of the charts of patients discharged with a primary diagnosis of diabetes mellitus will contain a recorded funduscopic examination."

5. *The education program must be implemented.* We may decide on a series of three presentations, one on classification of diabetic retinopathy; one a presentation of fundus photographs and/or clinical experience sessions; and one on photocoagulation techniques with laser beam.

6. *Finally, we must evaluate the program* at an

ppropriate interval. In our example, we study he next 100 consecutive records of patients ischarged with a primary diagnosis of diabetes nd determine the number of recorded funduscopic xaminations. If actual performance remains at 6 percent, our program failed; while if funduscopic exams jumped to 82 percent, we caused a hange in learner behavior.

What are the *requisites* for a hospital staff to erform medical audit? First, they must be *fficiently organized.* The common practice we ncounter is *horizontal* review of care rather than *ertical* (holistic or patient-centered). We have ften recommended a reorganization of medical ommittees with the anchor committee (called the udit or professional activities committee) systematically reviewing profiles of patient care.

Second a medical staff must have a medical ecords department capable of *information retrieval* on demand. If an audit committee of six nen decides to study the management of diabetes nellitus by reviewing all the charts for one year, hey might first decide what basic information hould be recorded on *all* diabetes charts. This nformation can be quickly provided by the nedical record librarian from the computer printuts (PAS/MAP). Then they might select for leeper study a certain group of diabetics which re displayed in groups on the computer printuts. Having decided to look at diabetes either roadly or at a specific problem in diabetes, the committee first sets *pattern criteria* for optimal performance, then goes to the records to see how ctual care measures up to optimal standards. The information they need to review care may be divided into: (1) that which the medical record librarian can get from the PAS/MAP computer printouts (example: percent of funduscopic exams), (2) that which the medical record librarian can find by studying the chart (example: percent of diabetics taught foot care), and (3) that which requires medical judgment and hence review of the record by a physician (example: appropriateness of the surgical therapy of diabetic peripheral vascular insufficiency). In this way, the committee can systematically review the care of diabetics in their hospital to determine what continuing education in diabetes is most appropriate for their medical staff.

In *organizing* medical audit, *only* the medical staff can establish optimal standards. The medical records department prepares the displays of actual care. The medical staff then performs the evaluative step by comparing the optimal with the actual level of care to detect gaps which may be closed by continuing education.

In addition to working with individual hospitals to assist them to institute audit, we have conducted monthly medical audit workshops using a "show and tell" format in which various hospitals present audits. Nurses were included initially, but now have split off into a separate group to develop nursing audits. We accept this split as a temporary expedient, and plan to bring the health team together by focusing on *patient-centered* (vs. professional-centered) and *outcome-oriented* (vs. process-oriented) audits.

In addition to the workshops we sponsored two more formal conferences: The first of these was the First Annual Minnesota Hospital Staff Conference in September, 1971. This two-day invitational conference was attended by management teams made up of trustees, administrators and key medical staff leaders from each of 27 hospitals. The theme of the conference was the quality of medical care in community hospitals. Its objective was to convince trustees that the responsibility for quality was legally theirs, and that they discharged this responsibility through the organized medical staff. We followed this up with a two-day continuation course at the University of Minnesota on the "how to" of medical audit in October, 1971, attended by 63 physicians from hospitals all over the state. We feel these companion efforts have helped to create a broad climate of acceptance of medical audit in Minnesota, and have developed a cadre of physicians capable of leadership.

Results

It is premature to evaluate the success of the first year's effort. We intentionally structured the program loosely to permit great diversity of activity among the participating hospitals. We felt the program would be more likely to succeed if it was their very own rather than a University program in their community. Because each hospital is so different politically and organizationally, the program took different forms at different sites.

Despite operational obstacles, and thanks to dedicated work by the DCME's and small staff committees, the first year's hospitals developed skills in medical audit, learned to develop their own pattern criteria, and learned to formulate education programs for the medical staff in re-

sponse to specific gaps identified by audit. They accomplished dozens of audits despite heavy patient care demands. Education programs were produced and when an outside speaker was employed, he was informed of the educational objective before he spoke to the staff. Time has not yet permitted completion of the audit cycle to see if the education resulted in change of physician behavior by re-audit of the disease or condition. We await these re-audits with great interest.

Subjects dealt with by the first year's hospitals included the use of antibiotics, anemia, diabetes mellitus, myocardial infarction, appendectomy, hypertension, duodenal ulcer, cholangiography, cholecystectomy, the use of tranquillizers, and urinary tract infection. In some instances data were pooled and shared by the hospitals.

Two hospitals, in auditing myocardial infarction, concluded that pacemaker capability was necessary for optimal care. As a result, members of each medical staff returned to the medical centers for training in the use of transvenous pacemakers. Another hospital, after auditing myocardial infarction, decided they needed to know more about serum lipids, and instituted a series of medical staff education sessions designed to improve their diagnosis and therapy of hyperlipidemia.

Audits of diabetes mellitus led one hospital to institute a series of educational programs on recent advances in the therapy of diabetic retinopathy. They selected this topic after discovering that only 34 percent of the patients discharged with a primary diagnosis of diabetes mellitus had their fundi examined. Another hospital concluded, after studying their diabetic care, that they needed to increase the use of other health professionals (nurse and dietitian) in the education of the diabetic patient.

Almost every audit disclosed room for improvement and indicated a specific behavioral change that was desired. The medical staff felt that an educational program would produce the desired result in some cases; in others, they chose a procedural or operational solution.

Discussion

We can generalize about a few things we learned in the first year:

1. Before action occurs, an attitude change must occur. We have seen a general acceptance of the peer review process, and of the concept that the organized medical staff is responsible, *as a group,* for every single patient cared for in the institution.

2. Medical staff organization is a problem. The medical care appraisal function is spread about in many committees and each hospital must solve this problem in its own way. Some redesigned their committee structure, others left the committee structure essentially intact, and reassigned functions. Common to all, however, was the perception of a *need to be organized* to accomplish the job of medical care appraisal.

3. The state of medical records is a problem. Since medical audit requires "the evaluation of medical care *as reflected in medical records,*" the record becomes the key document. If the record is complete, legible and contains a concise discharge summary, the record librarian is able to abstract it for PAS/MAP. The latter step permits another chance for error, however, and we learned that the record abstract was often the weakest link in the information retrieval chain.

4. Definition of optimum criteria by the medical staff is a problem. They are much more inclined to simply "take a look at a subject and see how we're doing," without having first defined standards. The criteria committees often asked for "cookbook" standards developed by "the experts," and had to learn that the educational value of standard setting probably equals that of care evaluation.

In addition to continuation and expansion of hospital-based medical audit, we plan to extend our program activities this year. Beginning April 1, 1972, Northlands Regional Medical Program has funded demonstration projects to extend audit to: (1) the outpatient setting, and (2) the problem-oriented record. These new directions recognize and attempt to correct two limitations of hospital-based medical audit. The first is that hospital-based audit does not apply to the medical care which takes place in ambulatory settings. Three group clinics (East Range Clinic, Virginia; Nicollet Clinic, Minneapolis; and the St. Louis Park Medical Center, St. Louis Park) have been funded to carry out computer-based audits of outpatient care this year, and we look forward to their results with great interest.

Audit of the problem-oriented record attempts to correct a second deficiency of the conventional hospital medical audit—namely that it accepts the diagnosis as given, and is unable to critically study diagnostic process or outcome. By auditing *prob-*

lems rather than *diagnoses,* we can set criteria for and evaluate the care of 100 consecutive admissions for *chest pain* or *headache,* or *jaundice, etc.* This strategy moves us closer to the real world of patient care and offers exciting opportunities for doctors to apply the educational process to their own logic sequence in patient management. Two hospitals (Bethesda Lutheran and Miller in St. Paul) began these demonstration projects on April 1, 1972, and we will be greatly interested in their results.

Summary

Northlands Regional Medical Program has begun to develop a system of continuing medical education based on needs demonstrated by the process of medical audit. This system offers the potential to: (1) increase the *relevance* of continuing medical education by relating it to patient care, (2) provide on-site learning experiences in community hospitals, (3) merge continuing medical education and patient care by making the community hospital a teaching hospital, and (4) above all, improve patient care through continuing medical education.

A Dialogue with Sir William Osler on Postgraduate Education

Critique of a Northlands Regional Medical Program

RUSSELL V. LUCAS, JR., M.D.

IT WAS A TYPICAL August night in Minnesota, sultry, wind gusting, sheets of rain assaulting my window and distorting the lights occasionally appearing in the inky black. I had labored some time, in vain, to prepare an evaluation of "A pilot project in postgraduate education in pediatric cardiology and neonatology." My friend Win Miller was acting like an editor. All creativity had escaped. I gazed vacantly out the window.

A rich warm voice projected from the shadows. "I had an interest in postgraduate education, perhaps I can help." I turned to see a tall slender man of impressive bearing. His black hair was beginning to recede, a full moustache adorned his upper lip, and his black piercing eyes were set off by full brows and an acquiline nose. Despite his appearance, he seemed a warm and understanding man.

Sir William Osler.

During the discussion that ensued, I had the wits to take some notes which I used later in recording our conversation.

Introduction

Sir William:

"Before we get down to your problem, what is the state of medicine these days?"

Author:

"Not too well if we take at face value what is described by the press, the 'lay medical journals', and politicians of all callings. They lament the widening gap between medical capability and medical performance. We hear, for example, that ⅓ of recent medical school graduates fail to continue postgraduate training once they start practice.[1] Estimates suggest that 20-70% of all M.D.'s fail to participate significantly in postgraduate educational endeavors."[2]

Sir William:

"Things haven't changed much then! Let me recall what I thought about that at the turn of the century. Bear with me if I falter occasionally; you're aware that we don't remember what we write.*

> If the License to practice meant the completion of his education, how sad it would be for the practitioner, how distressing to his patient.[3]

I was moved to sadness by a physician of my acquaintance who

> crawled up on the bank and the stream left him there, but he did not know it.[3]

On the other hand, the country doctor who maintained his skills and utilized his opportunities for postgraduate education filled me with joy."

Author:

"You're implying that the physician, now as then, lacks appropriate motivation for continued learning."

Sir William:

"Some perhaps, but that's not the whole story. What about the professor, the medical school, who are bypassed by the stream of medical knowledge. I used to call that condition 'old fogeyism'.

> Would you know the signs by which, in man or institution, you may recognize old fogeyism? There are three; First a state of blissful happiness and contentment with things as they are; secondly a supreme conviction that the condition of other people and other institutions is one of pitiable inferiority; and thirdly, a fear of change, which not alone perplexes, but appals.[3]

Are these signs of old fogeyism in today's pro-

This report is based on a demonstration project entitled "Pilot Study in Postgraduate Education in Pediatric Cardiology," sponsored by the University of Minnesota. It was a component of Northlands Regional Medical Program, Inc. supported by HEW grant #5 GO3 RM-00021. The opinions presented do not constitute endorsement by NRMP, Inc., or by the Department of Health, Education and Welfare.

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*Direct quotes from Sir William's writings are in references. Other comments are poetic license, but reflect the author's understanding of Osler's philosophy.

fessors and medical schools?"

Author:

"Yes, in some the condition is quite advanced."

Sir William:

"Then perhaps faulty postgraduate educational methods play an important role in the failure of physicians to participate in postgraduate educational opportunities."

Author:

"We thought so! In our design of a pilot study in postgraduate education in pediatric cardiology. we started with the assumption that faulty educational methods were a major factor. We believed that our own past efforts and others failed because they:

a. did not identify the needs of the learner-physician;
b. allowed little active participating by the learner-physician;
c. too often provided a mass of unintegrated facts;
d. did little to develop analytical abilities or judgment;
e. did not allow the acquisition of new skills; and
f. were seldom conducted in the physician's natural environment."*

Sir William:

"Well, Well. What's necessary for good postgraduate education then?"

Author:

"We thought the following:

1. The specific needs of the practicing physician must be identified and the curriculum designed to meet them.
2. The practicing physician must actively participate in the learning process.
3. The postgraduate program must be personalized so that differing needs of individual physicians may be met.
4. A significant portion of the program must occur in the physician's local environment.
5. The program should be patient oriented.
6. The program must be conceived as continuing over the professional lifetime of the physician."

Sir William:

"I see. You're trying to switch from a teacher oriented curriculum to one that's oriented toward the physician learner. How did you go about it?"

Author:

"The Northlands Regional Medical Program, a federally funded, regionally directed organization liked the idea, modestly funded us, and helped us define the following goals:

1. Provide immediate postgraduate education in pediatric cardiology throughout Minnesota;
2. Established more effective methods of postgraduate education; and
3. Encourage local physicians to assume a larger role in their postgraduate education."

Sir William:

"You call $30,000 a year modest! I recall when little more than twice that, $70,000, was the total budget for all 11 Canadian medical schools.[4] My apologies! Let's hear how you attacked those worthy goals."

Methods and Results

A. Utilization of the Crippled Children's Service Cardiac Clinic as a focus for Postgraduate Education

Author:

"Through the encouragement and cooperation of Dr. Mildred Norval, arrangements were made to utilize the crippled children's cardiac clinics as foci for postgraduate seminars. In our three year experience, thirty crippled children's cardiac clinics in nine Minnesota communities were utilized. In each of these clinics, 15-75 children with cardiac disease are seen. The clinics are staffed by pediatric cardiologists from the Mayo Clinic, St. Louis Park Medical Clinic and the University of Minnesota. A number of different educational programs were utilized in conjunction with the crippled children's cardiac clinics over the period of the pilot study as follows:

1. Informal lectures.

   An eight session curriculum designed to meet the needs of the practicing physician in the area of pediatric cardiology was formulated and utilized. This gave the visiting pediatric cardiologist guidance for his discourse and eliminated the possibility he would talk about his favorite defect or his current research efforts. The lectures were given during noon lunch breaks at hospital staff meetings, in the early afternoon at the cardiac clinics, in the late afternoon at the cardiac clinics, and at night after dinner and in conjunction with county medical society meetings. The noon and early afternoon sessions were least well attended."

Sir William:

"Perhaps practicing physicians are still busy in their clinics and miss lunch."

*Editor's Note: These several points apply to all phases of medical education!

Author:

"That's right. On the other hand, the late afternoon and evening sessions, though better attended, had a rather high percentage of inattentive physicians."

Sir William:

"Hypoglycemic and sobriety factors, respectively."

Author:

"Our next method was:

2. Patient oriented case discussions after cardiac clinics. These sessions allowed the physician to participate in the examination of a child with congenital cardiac disease and discuss the details of management. In one variation, patients with interesting and common problems were held over and presented to the physicians for their examination and discussion. This was a most valuable exercise if there were a small number of physicians. However, if more than 3 or 4 physicians attended, a great deal of time was wasted while each patient was examined and the sessions lost clarity and direction. For a small number, this type session was a most effective educational device. A second variation, useful for a larger number of physicians was to present the history and physical findings, review Xrays and electrocardiograms of a number of patients. Each case was the basis of discussion, often spirited, of the problems posed to the practitioner."

Sir William:

"That sounds better. The focus is now on the patient."

Author: "Our next approach was:

3. Physician attendance at the crippled children's clinic.

   The practicing physician often visited the cardiac clinic to review the findings and management of a patient he had referred. This provided an opportunity to review thoroughly the physical findings and the natural history of the cardiac disease and its management."

Sir William:

"Now you're getting somewhere! You've rediscovered the perfect medical learning situation, the triangle of student-patient-teacher."

Author:

"This was unquestionably the best learning experience, but it takes one teacher for every student. That's an expensive method."

Sir William:

"Perhaps, but do all your teachers teach? I doubt it. Some won't. Others, who will, aren't asked. This looks like a problem money is not required to solve, but rather harmony and good will in our profession.

> Medical men, particularly in smaller places, live too much apart and do not see enough of each other. In large cities we rub each others angles down and carom off each other without feeling the shock very much . . . as a preventative of such a malady, attendance upon our annual meetings is absolute, as a cure it is specific."[4]

Author:

"Perhaps then, even if some of our pedigogical methods were suboptimal, the fact they encouraged physician dialogue was most important."

Sir William: "Quite so."

Author:

"Sir William, your words about the isolation of physicians brings to mind a totally unexpected result of our educational efforts in the crippled children's clinics. It has to do with:

4. Education of allied health personnel in the Cardiac Clinics. Early in our program, the public health nurses and social workers in the cardiac clinics asked for educational sessions tailored to their needs. They were aware of the many problems faced by the community in providing the optimal environment for children with heart disease. Therefore, community school, hospital and public health nurses, social workers, and school administrators, teachers, and athletic directors were invited to special sessions at the close of the cardiac clinics. Brief explanations of congenital heart disease and rheumatic fever were given followed by a lengthy question and answer period. The discussions centered on the child with heart disease; his habilitation and rehabilitation, special school and activity programs required, his medical, dental and nursing needs, as well as the psychological stress imposed on the children and their families."

Sir William:

"Those are the things we doctors used to take care of."

Author:

"That's true, but most physicians today welcome this help. The major problem, as it is in all human affairs, is meaningful communication. We saw evidence that avenues of communication be-

tween the allied health personnel, parents, community physicians and medical center physicians were unclogged by these shared educational experiences."

Sir William:

"So you had 30 of these educational programs in nine Minnesota communities. How many students?"

Author:

"180 physicians, and 290 nurses and other allied health people."

Sir William:

"May I ask two critical questions. First regarding the scope of the program. I recall that I once said pediatrics was the best specialty, because children's ailments were too diversified to allow much specialization.[5] But pediatric cardiology; isn't that splitting the hair pretty fine?"

Author:

"That we learned. The NRMP people thought so, too."

Sir William:

"Secondly, while the cardiac clinics were in the physician's community, they weren't really in his practice environment.

> About the hospital centers all that is best and highest in the profession of medicine. In it, not in the medical school proper, not in the laboratories, not in the museums, we doctors live and move and have our being."[6]

Author:

"We recognized the validity of both of your critiques. Therefore, in 1970 we embarked upon a program to provide postgraduate education in the care of the sick infant in community hospitals."

B. In-service Training for Nurses and Physicians in Neonatal Intensive Care

Author:

"Several factors favored utilization of infant care as a focus for an in-service educational program for physicians and hospital personnel. These included the recent improvement in definitive care for infants born with serious cardiac defects and other congenital problems, the almost revolutionary improvements in supportive care for infants, the need for the acquisition of new technical skills, and new treatment philosophies in the care of infants. Further, since the infant has a limited response to illness, the techniques of medical care necessary for the infant with serious cardiac disease applied equally well to all who are sick. The goals of our in-service program were to:

1. Impart the knowledge and skills necessary to the recognition of the sick infant.
2. Provide the knowledge and skills necessary for appropriate therapy in the areas of oxygenation, heat control, feeding, acid base and electrolyte balance, treatment of infections, and treatment of congestive cardiac failure.
3. Provide the means to determine when a sick infant requires transfer to a specialized diagnostic and treatment center and the methods of optimal transfer of the infant.

An in-service training program, lasting one-half to one day was given in 21 hospitals. Each program was conducted by a physician and an infant intensive care nurse from the University of Minnesota Hospitals. Preliminary discussion between the visiting team and the community hospital personnel established the specific local situation and problems within the context of the above goals. In the 21 hospitals, 380 nurses, LPN's, and technologists and 45 physicians were served."

Sir William:

"I suppose it is still true that many of the new and specific medical facts and skills are soon obsolete."

Author:

"True enough. Important as these new facts and skills were, a more important consequence of the in-service programs was the establishment of improved communication among nurses, technicians and physicians. We also observed that the University nurse-doctor team improved their understanding of infant care."

Sir William:

"The teacher usually accrues the greater benefit in his encounter with a student."

Author:

"Evidence that improved patient care resulted from these programs can be found in several areas. Changes in nursing and hospital procedures were often instituted during and immediately after the in-service session. Several institutions sent one or more nurses to infant intensive care units for long-term training. Finally, there was a significant increase in the number of sick infants referred to neonatal centers in Minnesota and an equally dramatic improvement in their initial recognition, local care, and transport.

Sir William:

"These programs represent considerable effort. I'd be interested in knowing the participants."

Author:

"The NRMP through funding and by helping us to continuously refine our goals, and evaluate our progress. The Division of Crippled Children's Services, director, and clinic personnel, made the cardiac clinics possible. The Minnesota Chapter of the AMA, the Minnesota Chapter of the Academy of General Practice and the State Board of Health provided approval and support.

The County Medical Societies and the hospital staffs, provided their meeting times and facilities for our programs. The St. Louis Park Clinic, the Mayo Clinic, and the University of Minnesota, provided the teachers pediatric cardiologists and nurses for all the programs."

Discussion and Conclusions

Sir William:

"It would appear you and your colleagues have achieved modest success in reaching your first two goals. You have carried postgraduate education into Minnesota. You also seem to have instituted some improved methods of postgraduate study.

But what have you done to encourage the physician to assume greater responsibility for his education? A physician should return to formal study for several months every few years. During all my tenure at John Hopkins, I held courses for practicing physicians.

> To meet these good earnest students from all parts of the country, some of whom have been in practice fifteen or twenty years, stimulates ones optimism as to the outlook of the profession."[3]

Author:

"We must admit to failure in this regard, Sir William. In three years, only one physician availed himself of this opportunity to return to the University for one or two months, even with a modest stipend provided for study. Perhaps our offering was too specialized. Perhaps we did not "sell" hard enough. It may be physicians don't wish to shoulder the responsibility for their own continuing education. Many it seems, hand over this most important responsibility to others, their societies, their journals, their medical schools."

Sir William:

"A little harsh, don't you think, on both student and teacher? As I once predicted, medicine in the U.S. provides the world's keenest inspiration."[3]

Author:

"Sir William, your life and writings reflect a remarkable sensitivity to the medical needs of your time. This sensitivity to your own era, accounts no doubt for your unusually accurate prescience of our present time. Would you care to predict what lies in store for medicine in the U.S. today?"

Sir William:

"Recall that I've said few men over 40 retain their creativity. It's been a while since I passed that milestone. Moreover, the mark of an old, perhaps wise, man is to know when to quit. However, an old fool seldom can resist the chance for a final word.

First, postgraduate medical education is too important to be left to the professors, or to the societies, or to the journals or to the government. It must be nurtured, like life itself, by each physician. He must accept all the help he can get, searching always for the defects in his knowledge, the faults in his reasoning.

> I would encourage him in a keenly skeptical attitude . . . ever remembering Benjamin Franklin's shrewd remark that 'he is the best doctor who knows the worthlessness of the most medicines.'[7]

Second, all augers well for American medicine as long as it retains the excitement of discontent, the tumultuousness of conflict, the ecstasy of discovery, and the humility of commitment.

Finally, each physician marches to his own drum. Learn the beats of your colleagues, so as to understand them better, and to more fully appreciate your own beat."

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A Biomedical Library System for Minnesota

MARY JANE RYAN, PH.D.

BILLIONS HAVE been spent on medical research in this country, leading to a rapid expansion in medical knowledge. Still, the published information based on the research findings remained largely inaccessible to practitioners on the patient care level until more effective methods of retrieving the pertinent information were developed.

The purpose of this paper is to describe achievements to date in the development and extension of a biomedical library system capable of reaching practitioners in every region of Minnesota. The components of this system include: (1) the hospital library; (2) a local library supervisor; (3) library consultant services; (4) extension services from key libraries in Minnesota; (5) access to resources from the National Library of Medicine.

The main goal is to improve, equalize and expedite access to published literature in the health sciences. By linking and sharing the existing library resources at key centers, auxiliary library services become accessible to health professionals in hospitals and other health care institutions in other locations. The implementation of this concept is dependent upon close cooperation between the lending and the borrowing libraries and their parent institutions. In Minnesota there is a long tradition of cooperative arrangements between metropolitan hospital libraries and resource libraries sponsored by the University of Minnesota, the Mayo Clinic and by the Ramsey County, St. Louis County and Hennepin County Medical Societies.

However, health care practitioners outside of Duluth, Rochester and the Twin City areas have had limited access to medical and hospital library services. The priority accepted by Northlands Regional Medical Program is to help interested hospitals located outside metropolitan areas to develop effective library services pertinent to local staff needs.

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Dr. Ryan was Liaison Librarian, Northlands Regional Medical Program, Inc., St. Paul, Minnesota. Dr. Ryan died September 7, 1972.

The Role of a Hospital Library in a Small Community Hospital

The hospital library and its services should be developed to support the programs of the hospital and to meet the needs of the medical and hospital staff. Centrally located, realistically funded, adequately supervised, it should be available twenty-four hours per day.

A highly selective, relevant library is graphic evidence that a hospital cares about improved patient care. It probably represents the most important single facility for continuing education related to the delivery of optimum health care services.[1] Increased demand for expanded library services is stimulated by staff involvement in medical education, inservice education, field training, clinical staff meetings, accreditation committees, refresher courses, board examinations, peer review, medical audit, program development, community health, research, and preparation of talks and papers.

As the center for on-site information services, the hospital library must also function as the connecting link for interlibrary services from larger resource libraries.

The Hospital Library Committee, composed of physicians, nurses and other allied health professionals, can tailor the library collection and services to local needs, thereby making them truly viable resources.

Developing and Improving the Hospital Library Collection

Hospital libraries in small community hospitals do not need and should not have a large quantity of books and journals. What is needed is a current, basic collection of authoritative, relevant books, journals and reference materials which feature indexes. All major fields related to health care should be represented in the collection.

Paradoxically, one of the most obvious needs in the development and improvement of a hospital library collection is often the most difficult task to perform by local staff members. Discarding outmoded, mediocre, irrelevant material is more

difficult than selecting current, authoritative, pertinent books and journals. To thoroughly weed an existing library, each item should be scrutinized according to valid criteria: comparative merit, need, use, age and value.

Most literature pertaining to health care is of dubious value within five to ten years of publication. An old book in most fields of clinical medicine is more than worthless. If it contains obsolete information, it often is downright dangerous. It is no longer necessary for a small hospital library to retain retrospective journals beyond five years. By interlibrary services available from the Bio-Medical Library of the University of Minnesota and from the Mayo Clinic Library, photocopies of articles needed can be procured at a nominal fee.

Periodical Indexes

Money spent in embalming restrospective journals in buckram can be more wisely invested in subscribing to a few key indexes. Serious consideration should be given to subscribing to three basic indexes. For approximately one hundred dollars, CUMULATIVE ABRIDGED INDEX MEDICUS,[2] CUMULATIVE INDEX TO NURSING LITERATURE,[3] and HOSPITAL LITERATURE INDEX,[4] for 1970-1972 can be procured. This expenditure will allow the hospital staff bibliographic access to approximately 600 journals—all containing potentially relevant articles on health care delivery.

Indexes to the journal literature perform a dual function: (1) they are the best tools for retrieving needed information from locally available journals; and (2) they are the keys to obtaining citations to needed articles from resource libraries through interlibrary loan services.

Journal Selection

Like books, locally available journals should be representative of the major fields of clinical medicine and the patient care given at the hospital. Valid criteria for journal selection must include a comparative analysis of several journals in the same field. Other criteria of parallel importance involve price, availability with memberships, and whether or not the journals are cited in the periodical indexes. The larger the hospital, the larger the professional staff, the more teaching and research conducted, the more journals which will be needed and hence, the CUMULATED INDEX MEDICUS, 1960+ should then be provided.[5]

Book Selection

One of the best methods of book selection is to obtain two or three current, authoritative titles in the same field on approval from a publisher, his agent, or a medical book store. By content analysis, an experienced health professional can make a valid judgment on selecting the best text to supplement existing local material and to meet the needs of local hospital professionals.[6]

Core Library Loans

Since May, 1970 Northlands RMP has loaned five model libraries to 76 hospitals requesting this service (Figure 1). In every instance the loan stimulated new book purchases by the hospital. Two of the lists, the CORE MEDICAL LIBRARY[7] and the CORE NURSING LIBRARY,[8] were developed at the Postgraduate Medical Institute of Boston by Stearns and Ratcliff. The IOWA CORE LIBRARY list —geared to the small community hospital—was developed by the Iowa Regional Medical Program. The EMERGENCY CARE LIBRARY and the INTENSIVE CORONARY CARE UNIT SHELF lists were developed in Minnesota by Northlands RMP and Minnesota Heart Association respectively. To maintain currency, new editions are added upon publication.

The Library Supervisor in Small Community Hospitals

Most hospitals under 300 beds cannot afford to employ a full-time professional librarian. However, every hospital should appoint one employee to serve as library-supervisor, and with this ap-



Figure 1

pointment, allocate adequate time to fulfill the responsibilities involved. A successful combination of duties has been a half-time librarian and a half-time secretary to a Director of Continuing Medical Education, or to the Director of Inservice Education. When deliberately sought, a local resident with library training or experience can frequently be found. A half-time position as a hospital librarian often appeals to a young married woman in the community.

Library Workshops

Under Northlands RMP sponsorship and at the invitation of hospitals, one-day workshops on hospital librarianship are being held in every region of Minnesota, (Figure 2).

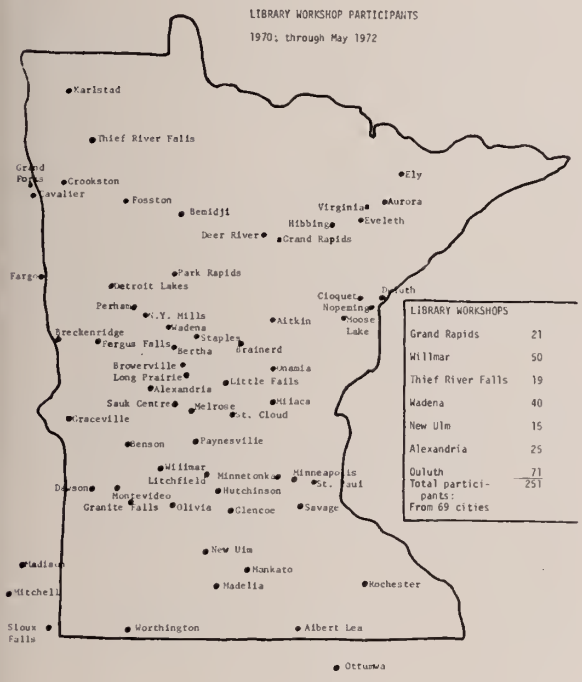


Figure 2

Not every hospital has an employee designated as library supervisor. Frequently participants at hospital library workshops are members of a hospital library committee, including physicians, hospital administrators and nurses. Stimulated by a sincere desire to learn more about developing and improving hospital library services, they come to learn about the basic elements involved—including the need for local library manpower and for funding the services. In order to be effective, library workshops must involve staff members who make final decisions about the development and improvement of hospital libraries.

Invitations to workshops are issued to nearby hospital administrators and identified health professionals who have requested library services from Northlands. Workshop participants come from several disciplines including physicians, nurses, administrators, therapists, technicians, medical records personnel, secretaries and librarians.

The agenda for each workshop varies somewhat depending upon the needs, interest, jobs and backgrounds of registered participants. Generally, two broad subjects are presented: (1) organizing and maintaining a local library service; (2) obtaining interlibrary services from the Mayo Clinic Library and the Bio-Medical Library at the University of Minnesota. A take-home kit is provided for further self-learning.

Apprenticeship Training

To meet a specific need for a deeper, more comprehensive training in hospital librarianship, apprenticeships have been arranged upon request by Northlands RMP. Supervised hospital library field work provides a tutorial learning experience in an ongoing library for a half-time hospital library employee. The field experience is matched as closely as possible with the needs of the new employee and her duties to her clientele at her base hospital. Matching elements include: size of hospital; size of medical and hospital staff; patient care; services; education programs; teaching programs; geographical location; long-term goals for library services; proximity to a model library and to an experienced, fully-qualified hospital librarian.

Short-term apprenticeships can be arranged for a one or two-week period. When feasible, arrangements can be made for a new hospital librarian to commute one day per week over an extended period of several weeks to receive on-the-job training from a nearby hospital librarian.

The quality of library services given is directly related to the motivation, ability and training of the person functioning as librarian. No one can function effectively without proper orientation and training.

Consultant Services

Since every hospital cannot have a professional librarian, consultation services of a certified medical librarian are frequently needed. The Liaison Librarian of NRMP has provided this service to over 112 hospitals and clinics in Minnesota and adjacent areas since 1970. (Figure 3). The re-

quests show a crucial need for expert help in developing and improving hospital libraries outside the urban areas. Consultations have been held on the following problems: planning and redesigning library facilities; evaluating and discarding local materials; organizing materials; developing multi-media services; establishing policies of services to students receiving field training; revitalizing the library committee and establishing short-term and long-range plans for expanded services.



Figure 3

Many talks have been given, upon invitation, to medical societies, hospital and clinic staffs, hospital administrators, nurses, medical technicians and medical record personnel.

These encounters lead to varied and multiple requests for extended library services from Northlands and from the medical center libraries, as professional staff become aware of their availability. The majority of requests are filled through correspondence and by telephone, as they pertain to specific materials or information.

Medical Library Assistance Extension Act of 1970

Medical Library Resource Grants authorized by the Act are meant to stimulate local support for upgrading library resources or services. The Improvement Grant program is directed to hospitals and health care institutions which need to establish a library or to improve and expand their basic resources. It is a one-year, nonrenewable grant in an amount up to $3000. An application kit, which includes a policies and procedures manual, is available from National Library of Medicine, Extramural Programs, Resources Division, Bethesda, Maryland 20014.

As of July 1972, sixteen health care libraries in Minnesota received funded grants under this Act. Six applications are pending and another eighteen health care institutions have written for the application material.

Extension Services from Mayo Clinic Library and Bio-Medical Library

To meet the increasing demands for interlibrary loans and other services from hospital libraries and their users, the position of Extension Librarian was established at both the Mayo Clinic and the Bio-Medical Library in September, 1970 (Figure 4). These Extension Librarians handle all requests from libraries and health professionals in outlying areas of Minnesota. By tapping their own resource library either Extension Librarian can supply materials needed by practitioners in any locale.[9] The Extension Librarian provides the link between the local library supervisor or practitioner and the resource libraries in Minnesota, Midwest Regional Medical Library in Chicago and the National Library in Bethesda, Maryland.

The two medical center libraries extend the benefits of their resources to all practitioners and health care institutions in Minnesota. The only



Figure 4

charges are a nominal handling fee plus photocopy costs. The rapidly increasing outreach services are shown in Figures 4 and 5 and the Table.



Figure 5

Biomedical Serials, 1972

To further simplify the procedure of obtaining a specific article from a specific journal held at either Bio-Medical or the Mayo Clinic Library, Northlands RMP published a joint list of the serials held by these libraries in May, 1972. The user of this volume can verify whether or not the desired journal is available at one or the other library. *Biomedical Serials, 1972* is distributed free of charge to Minnesota hospital or clinic libraries upon written request to the NRMP Liaison Librarian.

Computerized Literature Searches

Any practitioner in Minnesota can obtain a bibliography of the latest literature on any biomedical subject by requesting a MEDLINE search.

MEDLINE (MEDLARS [Medical Literature Analysis and Retrieval System] On-Line) is a national bibliographic search service available since June, 1972, to Minnesota physicians through the Bio-Medical and the Mayo Clinic libraries. By means of a computer terminal and a telephone link it taps a computerized data base initiated by the National Library of Medicine. The MEDLINE data base consists of over 400,000 articles from over 1100 health science journals cited in Index Medicus since January, 1969. To maintain timeliness, citations will be added and dropped annually.

At Bio-Medical Library, during the first year of MEDLINE operation, service will be limited to calls from practitioners outside the Twin City area. Practitioners in the metropolitan area can obtain MEDLINE searches through their local hospital or medical society librarians.

In order to request a MEDLINE search, an outstate physician can call the Minnesota Medical Information Service operator. (MMIS) toll-free at 1-800-552-7210.* The operator will ask for a description of the problem, record the information and forward the request to the MEDLINE librarian at the Bio-Medical Library. If necessary, the librarian will return the call to verify the interpretation of the problem. The bibliography obtained from the computer search will be mailed to the practitioner. Photocopies of specific articles can also be sent if desired. During the first year, there is no charge for MEDLINE searches other than the cost of photocopy at ten cents per page and a dollar handling charge per order mailed.

MEDLINE service is also available at the Mayo Clinic Library. For detailed information on Mayo services, contact the Extension Librarian, Mayo Clinic Library, 200 First Street S.W., Rochester, Minnesota 55901 or phone: 1-507-282-2511, Extension 2061.

TABLE
Library Extension Services from Biomedical and Mayo Clinic Libraries
1969 and 1971

Services to Hospital Libraries & Practitioners in Minnesota	Biomedical Library 1969	Biomedical Library 1971	Mayo Clinic Library 1969	Mayo Clinic Library 1971
1. Number of Hospital libraries loaned material located in Metro area	11	14	5	14
2. Number of Hospital libraries loaned material located in Outlying areas	8	32	2	20
3. Total number of requests filled for Outlying practitioners via hospital libraries & clinics	185	356	6	241
4. Total number of requests filled for Metro libraries: hospital, clinics	4275	7228*	21	584
5. GRAND TOTAL REQUESTS FILLED (items 3 + 4)	4460	7584	27	825
6. Literature searches & Bibliographies compiled for practitioners in outlying areas	—	108	—	40
7. Reference questions answered for practitioners in outlying areas	—	50	—	17

*Requests averaged 16 per day.

*MMIS is a central information service providing Medical Library Service, Dial Access Tapes, Drug Information and Medical/Dental Specialty Advice. It is sponsored by the University of Minnesota and partially subsidized by NRMP.

Summary

Since 1970, a cooperative effort has been made to improve, equalize and expedite aeeess to published literature for health professionals in Minnesota. To help interested hospitals with library development, the following services are available from Northlands RMP: core library loans; hospital library workshops; apprenticeship training and consultant services.

A nationwide network of biomedical libraries was established by the National Library of Medicine. All medical and hospital libraries are automatically part of this network. By linking and sharing existing library resources at key eenters, supplementary services become accessible to practitioners in hospitals and other health care institutions located away from large libraries. Medieal Library Resource Grants are available under the Extramural Programs, Resources Division of National Library of Medicine.

The Bio-Medical Library at the University and the Mayo Clinic Library, through their Extension Librarians, offer: interlibrary loans; photocopy services; reference services and literature searches. Through them, libraries throughout the nation can be tapped when needed material is not available within the state. The role of these resource libraries is to supplement—not supplant—the hospital library.

As the center for on-site information services, the hospital library must also function as the conneeting link for interlibrary services from larger resource libraries. The effectiveness of the biomedical library network at the patient care level is dependent on the quality of the hospital library.

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Patient Education in Community Hospitals

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OVERWHELMING DEMANDS are presently being placed upon the health care system of this nation. These forces seek to improve not only the quantity and quality of health care available but to simultaneously decrease its cost. The major response to these stimuli has been to train more allied health personnel who can quickly increase manpower capability at a minimal cost. In 1970 the ratio of allied health personnel to physicians was already 16 to one; and it is anticipated that by 1980, this figure will have increased to 25 to one.

Medical schools are being encouraged to escalate the size of their classes; two year schools of medicine have been expanded to four year programs and numerous new schools are being established. These methods of meeting expanding health care needs are merely an extension of an existing system where professional medical personnel assume a very active role in the treatment of a very passive patient.

The complex nature of today's health care needs demands a more comprehensive and creative approach. The leading causes of death today result from chronic illnesses such as heart disease, cancer, stroke, diabetes, respiratory and renal disease. These conditions require careful management over long periods of time. Merely increasing the number of health care professionals does not insure improved management of these chronic illnesses.

The greatest responsibility for health management lies with the patient himself. It is the patient who must carry out the day-to-day management of his illness while the physician and his co-workers must assume an advisory or supportive role. There has been little recognition or acknowledgement that the most important person in the health care system is the patient. In order for the patient or members of his family to effectively participate in management of a disease, they must understand their particular roles and responsibilities. Proper care of chronic diseases can only be achieved by informed patients cooperating with knowledgeable and interested professional personnel.

Recently several studies have been conducted to determine what the diabetic and his family know about the condition with which they live and assume significant responsibility.[1,2,3] The results were appalling, such as: More than 50% of the juvenile diabetics didn't understand acidosis and 50.4% didn't know the time-action of insulin they took each day. McDonald of the U.S. Public Health Service conducted a national study among diabetics and reported similar findings.[4]

In an effort to improve the patient and his family's understanding and knowledge of the disease, the Diabetes Education Center was established in Minneapolis. The Center serves as a regional resource where practicing physicians can refer their patients for indepth educational experience; and provides an educational program where professional health care personnel can obtain comprehensive training in the management and education of the patient with diabetes. The concept of patient education as an integral part of quality health care, however, is poorly understood and accepted. Consequently, a project was developed by the Minneapolis Diabetes Education Center to assist in investigating this aspect of health care. The program described here was conducted between June of 1969 and April of 1972.

Project

The objectives of the Diabetes Regional Center Project were:

1. To study current methods for delivery of health services to individuals hospitalized with a chronic disease.
2. To determine how this care can be improved.
3. To develop the necessary programs, materials.

This demonstration project was sponsored by the Diabetes Education Center, Minneapolis, Minnesota. It was a component of Northlands Regional Medical Program, Inc. Supported by HEW grant #5 GO3 RM-00021. The opinions presented do not constitute endorsement by NRMP, Inc. or the Department of Health, Education and Welfare.

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techniques, etc. for implementing such improved care.
4. To evaluate and summarize the experiences of the program in "key" hospitals.
5. To begin peripheralization of the program to small communities in the region.

Three hospitals were chosen to be studied during this project period. The first two hospitals involved, A and B, were chosen because they had differing locations, contrasting patient populations and needs. Hospital A is a new 378-bed general hospital located in suburban Minneapolis while Hospital B is an older 370-bed general hospital in downtown St. Paul. Both institutions had directors of medical education and administrators interested in patient education. The third hospital, C, is a 423-bed general hospital located in the central areas of Minneapolis. This hospital constituted a teaching and community service facility used by many different population groups and promised enthusiastic administrative support.

A Coordinator of Patient Education was hired for each hospital. Three of the four coordinators had nursing backgrounds and two had advanced degrees in health education. The coordinators chose not to stress their nursing backgrounds since this would identify them with traditional concepts and roles, thus limiting their staff and administrative mobility.

Since no previous guidelines were available, the job description of the coordinator had to be determined through trial and error.

The responsibilities of the Coordinator of Patient Education are now described as:

1. To become acquainted and identified as a resource.
2. To determine the educational needs of diabetic patients receiving care in the particular hospital.
3. To assess the resources and barriers pertaining to the establishment of a patient education program.
4. To devise a plan or system to initiate or improve patient education programs within the hospital.
5. To implement such a plan.
6. To evaluate the plan's effectiveness.

The Coordinators familiarized themselves with their respective institutions by attending meetings and conferences, visiting the floors, and participating in activities designed to acquaint them with all personnel. Simultaneously, they acquired information on the hospital's needs and resources. In Hospital A, for example, a survey of patient records revealed 194 patients were discharged with a diagnosis of diabetes mellitus over a four month period. Two-thirds of these were between 51 and 80 years of age with a ratio of 95 male to 99 females. Seventy percent were Protestant and all but one was Caucasian. The average length of stay was 11.5 days in contrast to 6.6 for the entire hospital population. The majority of these patients came from the surrounding suburban area where socio-economic characteristics revealed the population to be middle class, most of whom had a high school education and an average income of $7,000 to $15,000 per year. Patient teaching programs in diabetes had been initiated at the hospital in 1964, 1966, and 1968, but they encountered difficulty because physicians failed to order "education," and floor personnel forgot about the program.

Similar studies were carried out in each hospital to determine its individual characteristics and profile. All coordinators began by organizing an interdisciplinary committee on Patient Education. Committee members were chosen, volunteered, or assigned by administration. They included representatives from Nursing, Medical Staff, Occupational Therapy, Social Services, Laboratories, X-Ray, Medical Records, Pharmacy, Library, etc.

Despite employment within the same institution, the lack of communication among interdisciplinary groups represented on the committees was astounding. The first objective of each committee was to learn to communicate and function together as a group. All committee members also sought to increase their own knowledge of diabetes by reading; sharing reports; assembling diabetes literature; sponsoring, attending, and participating in lectures and conferences; as well as enrolling in the five-day educational course for allied health professionals at the Diabetes Education Center in Minneapolis.

With increasing insight into their own needs, each committee chose to assess knowledge of diabetes and its management among other members of the "health team" in their own institutions. For instance, one committe chose to evaluate the patient population and devised a 35-item test on diabetes. This was pre-tested on the institution's professional staff. Ninety-six percent of the staff thought the test suitable as a gross measurement of knowledge of staff and patients. The test results among the patients and professional groups are shown in the Table.

TABLE
Results of 35-Item Test on Diabetes

Residents/Interns:	Number Wrong	Score
Average	8	76%
Range	4-11	69-89%
Nurses:		
Average	9	78%
Range	1-16	45-99%
Patients:		
Average	18	49%
Range	7-35	0-80%

Each hospital conducted such studies which stimulated interest and inservice education activities. One institution organized a two-day symposium on diabetes for the medical house staff.

Initially, it was difficult to identify all diabetics being admitted to the hospital. Two institutions utilized the PAS system of record analysis. It was found however that "diabetes" was sometimes omitted from the admitting or discharge diagnosis, particularly when the patient was suffering from a multitude of problems. The most valid source of diabetes diagnosis in one institution was found to be the Medical Records office rather than Admitting, since the former tends to group patients in 24-hour collections while Admitting is continually adding to its list throughout the day. Cross-checks to pick up the "unidentified" diabetic in-patient may be made with the Dietary Department or the Pharmacy Department. "Diabetic Diet" orders or prescriptions for insulin or oral hypoglycemic agents may assist in locating these patients. Laboratory personnel also assist by reporting patients with elevated blood sugars. Once the institution becomes sensitized to identifying the diabetic patient, ward secretaries become the most effective and reliable resource. However, such cooperation and assistance is generally achieved only after a long period of institutional indoctrination, education, hard work and frustration.

At the time the program was initiated, there was only one diabetes teaching program in the three institutions. It had been initiated in the Spring of 1968. Seventy-two patients, or an average of six patients per month, had been referred to classes during the first year of operation. Only 56 patients had completed the series of five classes during the first 17 month period. Analysis of hospital records, however, revealed the *daily* hospital census ranged from eight to 20 diabetics. The program had no written objectives but it was assumed to be suitable for the newly diagnosed diabetic and those out of control. It was anticipated the program would be attended by members of the patient's family and by out-patients. However, attendance by family members had been disappointing and only one out-patient had participated. A charge was made for the course and in most instances this was covered by hospital insurance.

Once the Coordinators and their committees had gathered information on existing teaching programs, defined patient profiles and needs, assessed hospital barriers and resources, and increased their own awareness of diabetes and education, two of the hospitals initiated education programs and the third strengthened its existing effort.

Teaching Programs

The nature, content and extent of patient education programs to be conducted within each hospital had to be determined. The committees recognized that most hospitals were acute care facilities where ill patients are admitted, treated and discharged as soon as possible. It was generally agreed, however, that hospital in-patient teaching programs should include the following fundamental information of the disease and its management:

1. Basic concepts of diabetes.
2. Insulin and insulin administration *or* oral hypoglycemic drugs.
3. Urine testing for sugar and acetone.
4. Diet.
5. Acute complications (hypoglycemia and acidosis).
6. Personal hygiene.
7. Exercise.

It was recognized that extensive in-patient teaching programs should not be provided in most institutions because of (1) variations in individual patient needs and receptivity during hospitalization; and (2) limited time, personnel, finances and facilities. The presence of the Diabetes Education Center in the community provided a resource where patients could complete an indepth comprehensive educational program on an ambulatory basis at a minimal cost and during a more appropriate phase of their disease.

The need to individualize certain aspects of patient education was recognized. Group patient classes have the advantage of saving time and minimizing costs; but not all techniques and materials are effective for teaching all patients in a single class. In order to meet this challenge, two com-

mittees developed initial interview forms to be administered by professional persons upon patient admission, or when feasible. A self-assessment form was devised to determine what the individual patient does or does not know about his disease. This information plus the patient's medical history, nursing and nutrition interviews, and input from social service provided a wealth of information. It was necessary then to devise a plan to assess and exchange this data among participating personnel. Interdisciplinary patient care conferences, or PEP (Patient Education Planning) conferences as one institution chose to call them, were initiated. Team members exchanged data obtained both formally and informally, and an individualized patient education plan was devised. Information concerning such items as disease acceptance, visual status, dexterity, personality, economic problems, marital difficulties, language barriers, educational background, etc. were discussed Having pooled this data, the "teachers" then established realistic goals for the patient and the health care team.

Assistance in determining program content and teaching materials was obtained from the staff's own investigational activities and with guidance from the staff of the Diabetes Education Center. New props, plans, and programs were created by the individual institutions as they sought self-identification, expression, and acclaim.

Blocks and Pressures

Planning a teaching program is difficult even for a committee of interested and knowledgeable individuals. The greatest challenge, however, is to implement and maintain a health education program, for this requires institutional acceptance and commitment. Communication and cooperation were not always maintained on an interdisciplinary basis within the Patient Education Committees, and these were frequently not achieved even on an intradisciplinary level outside of the committee. Personality and political differences and concerns within a hospital reflect the same variations seen within the community. The charismatic individual who can be most effective in establishing teaching programs or instigating institution change is not always found in positions of power on the institution's Table of Organization. Conversely some of the greatest "blocks" may be applied by hospital "leaders" who feel threatened for one or another reason. Verbally, almost all hospital personnel agreed that patients should be taught. However, the depth of that conviction quickly became evident when the questions of cost and commitment were introduced.

As part of this study, one author chose to assess existing patient educational programs in 26 hospitals in the Twin Cities area. When the administrators of these hospitals were asked if their institutions provided programs for patient education, all replied "yes." When asked to identify an individual who coordinated these efforts or worked in this area, only 12 of the 26 institutions could produce a name. In most instances (58%), responsibility for patient instruction was defined as a function of the nursing service. Only 15 of the 26 hospitals reported having purchased any materials for patient education during the previous year. Only three institutions had any budget allocations made specifically for patient education!

Evaluation

As a consequence of this program diabetes teaching programs were initiated in two hospitals. In the third hospital innovations were made, and institutional awareness increased so that during the final four months of the study, patient attendance rose to an average of 14.5 patients/month with 23 family members, and 13 patients repeated one or more of the classes.

During the period of investigation one of the hospitals experienced a change in administrators; this resulted in an almost total loss of support for patient education. The committee in that institution was told to submit a budget for the following fiscal year; and although the work was verbally supported in committee hearings, the request for funds was denied. Portions of the committee still meet with a health educator at planned intervals, but "acceptance" of patient education within the institution is low.

One hospital not only accepted the concept of patient education but has established an independent Department of Health Education with a budget of over $300,000 a year. This hospital prides itself on this unique service to the community and has received national recognition. The following improvements[5] have occurred as a result of this effort:

1. Total hospital communications have increased because of interdisciplinary cooperation.
2. Staff members have been stimulated to increase and update their individual knowledge and skills.
3. A valuable stimulus for planning and implementing team projects has been provided.

4. Physical care of patients has improved.
5. Patient satisfaction has increased.
6. The institutional image in the community has been improved.

Peripheralization of this program has stimulated initiation of patient education teaching programs in many cities, towns, and institutions throughout the region and the nation. A standing committee on Regional Medical Programs and Diabetes Education Centers has been established within the American Diabetes Association as a direct result of this project, and a one-day program devoted to patient education is now part of the Annual Postgraduate Course of the American Diabetes Association.

The concept that the patient is an essential part of the medical team and that his education and cooperation are essential to quality health care is still rarely understood and poorly accepted. In September 1971 the President appointed a commission to study Consumer Health Education in this nation. The results of that study will probably be released sometime in the near future. Patient education and his incorporation into the health care team promises to produce one of the greatest impacts on health care of the decade!

Summary

Health care and needs are currently undergoing great changes. One of the greatest of these promises to be the involvement of the patient in his own health care. The establishment of Patient Education in Community Hospitals in order to provide patients with sufficient knowledge to become an effective member of the medical team is a difficult task. Experiences in three such institutions are described herein.

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Education of Non-Physician Personnel in Stroke Rehabilitation and Chronic Illness

ANITA P. SMITH, PH.D.

Implicit in the concept of rehabilitation is a commitment to provide continuity in patient care, not only in the hospital but beyond it. Physicians, because of their limited numbers and crowded schedules, cannot be expected to meet this need without the assistance of other informed persons in the community. In order to provide the additional health manpower required, it is necessary to train and use key resource groups, such as the clergy and family members, as well as to upgrade the technical skills of presently employed health professionals. The Sister Kenny Institute presented a means of realizing the goal of continuity in care of the stroke patient by educating nurses, social workers, the clergy and families to more effective ways of meeting the patient's physical and psychological needs.

Objectives

In March, 1969, the Sister Kenny Institute initiated its project on "Improving Stroke Rehabilitation Through a Regional Program of Continuing Education." The overall purpose of the program was to help provide improved and more comprehensive health care for stroke patients and other chronically ill or disabled persons by: (1) updating and upgrading the knowledge and skills of those involved in the patient's rehabilitation, and (2) augmenting available health manpower.

The specific objectives of this project were:

1. To increase the numbers of professional persons able to provide improved treatment and care of stroke patients.
2. To upgrade the technical skills and knowledge of health-related professionals regarding stroke and rehabilitation, emphasizing the broadened scope of activity possible in traditional professional roles.
3. To facilitate the development of dialogue and inter-institutional cooperation throughout the region in the joint effort required to improve the care of stroke victims.
4. To further the knowledge and understanding of the regional lay public, especially the families of stroke patients, regarding the medical and psychosocial aspects and implications of stroke as related to the treatment and care of the affected family member.

Project Description

This project consisted of six independent but related programs of continuing education, all offered over a three-year period from March, 1969, to April, 1972. Three in-depth courses were offered at the Sister Kenny Institute, Minneapolis, a total of 27 times: *Nursing Care of the Long Term Patient* (14 course offerings); *Social Work Refresher and In-Service Course* (five course offerings); and *The Clergy and Rehabilitation of the Chronically Ill* (eight course offerings). The *Community Nursing Education Seminars* (422 sessions) and *Stroke in Your Family* (22 seminars) were offered on-site as requested by individual institutions and local communities. The *Regional Service to Schools of Nursing* program was conducted only during the second year of the grant. Each course charged a nominal tuition fee to insure student commitment in attending with out-of-state applicants accepted but at a regulation tuition rate, e.g., $250 per student for *Nursing Care of the Long-Term Patient* (vs $50 for Minnesota students). Living stipends for out-state Minnesota students were available at $16 per day. A summary description of the project units can be found on the following page.

The faculty for these courses were recognized experts in their particular specialties. Included were physicians, social workers, psychologists, occupational and physical therapists, nurses, voca-

This demonstration project was sponsored by the Sister Kenny Institute. It was a component of Northlands Regional Medical Program, Inc. supported by HEW grant #5 GO3 RM-00021. The opinions presented do not constitute endorsement by NRMP, Inc. or the Department of Health, Education and Welfare.

tional counselors, speech pathologists and other rehabilitation professionals from the Kenny Institute, the University of Minnesota, community agencies and private practice.

All of the programs discussed here utilized a variety of teaching methods with the particular method used depending on the topic and type of material being presented. These included: lecture, demonstration-return demonstration, clinical observation, clinical practice, tours, attendance at patient-planning conferences, seminars, problem-solving discussions and individual study assignments. Audio-visual media such as films, filmstrips, slides, overhead transparencies, video tapes and closed circuit television were used throughout the courses to increase learning and retention.

Although program activities remained substantially the same in general purpose and structure throughout the three years of the project, certain changes did occur during that time. First, course objectives and content were broadened to apply to a wider scope of disabling conditions than stroke alone, e.g., heart disease, cancer, arthritis, spinal cord injury, etc. Second, the emphasis was changed from refresher and pre-service training in the *Social Work* course to in-service, as this need became apparent toward the end of 1970. Third, a team concept was introduced into the Community Nursing Education program with the addition of a physical therapist to the staff. Finally, it became necessary, due to decreased funding, to reduce project personnel time, eliminate expansion activities and offer fewer courses and seminars.

Project Evaluation

Evaluation methods for assessing the achievement of program objectives encompassed a considerable range of procedures. Student knowledge, skills, attitudes, performance with patients and changes in all these dimensions were examined. Criteria were established to determine successful achievement of each goal.

Criteria were defined quantitatively for those objectives dealing with increasing the number of stroke-sophisticated manpower and with furthering communication and cooperation among health-related professionals. The following were considered indicators of goal achievement: the number of students attending the courses; what geographical areas in the state they represented; and the number and types of participants from various disciplines who, by involvement in the courses,

SUMMARY OF SISTER KENNY INSTITUTE CONTINUING EDUCATION PROGRAMS

Course	Eligibility	Times Offered Annually	Class Limit	Length of Course	Course Content	Locale
Nursng Care of The Long-Term Patient	R.N.'s in positions of educational leadership	4-5	18	2½ weeks with an optional week of supervised practice	85 hours on nursing techniques, psychosocial understanding and communication methods to improve stroke care; also content for use in in-service education.	Kenny Institute for course: employing institution for in-service education.
Community Nursing Education Seminars (Field Education)	Community agencies, nursing homes, hospitals, and professional organizations	Arranged individually	Open	Arranged individually	Short training programs conducted by Kenny nurse-educator, on nursing techniques for patients with stroke and other long-term illnesses.	Local communities
Regional Service to Schools of Nursing	Any accredited educational program for vocational, technical, or professional nurses.	Arranged individually	5 or more nursing students accompanied by an instructor	3 hour seminars or 3-5 day clinical experience in long-term nursing care.	Lecture on role of the rehabilitation center and special nursing care of the patient with a long-term illness. Discussion of topic elected by the nursing school.	Kenny Institute
Social Work Refresher and In-service	B.A. plus social work experience or graduate credits in social sciences	1-2	15	2 weeks	42 hours of instruction on current methods and practice in social work, medical and psychosocial aspects of chronic illness, and community agencies and resources; 18 hours in clinical settings.	Kenny Institute
The Clergy and Rehabilitation of the Chronically Ill	Ministers, priests, rabbis, hospital and other professional persons concerned with religious implications of chronic illness.	3 times annually for 3 day course. Arranged individually for 1 day seminar.	20 for course	3 days for course 1 day for seminar	18 hours of instruction on medical and psychosocial aspects of chronic illness, community resources and role of the clergy.	Kenny Institute for course. Local communities for seminar
Stroke in Your Family	Families of stroke patients, physicians, nurses, and other interested medical personnel.	Arranged individually	50	1 half day as requested	Approximately 4 hours of instruction on medical aspects of stroke, communication, ADL's and community resources.	Local communities

broadened their traditional roles through new interactions and activities, e.g. teaching or supervising students.

Criteria for successful achievement of the project objectives concerned with updating and improving stroke knowledge, skills and practice of both health professionals and laymen were directly related to evaluation of the individual unit (course) objectives. Evaluation techniques for appraising achievement of goals included role-playing, problem situations, open-ended discussion, case studies and quizzes. Observation and rating of student-patient interaction and of task performance were utilized.

Results

Project Objective 1

To increase the number of professional persons able to provide improved treatment and care of stroke patients.

The number of nurses, social workers, clergy, other health professionals and family members who attended the continuing education courses and seminars offers conclusive evidence that this objective was achieved. A total of 20,392 students participated in the project during its three year existence for an average of approximately five hours of instruction per student. Of the total students, 405 attended the three in-depth courses at Kenny Institute with an average 65 hours of instruction per student. The outreach program of community education seminars, including *Stroke in Your Family,* involved 19,418 students from throughout Minnesota for an average four hours of instruction each. *Regional Service to Schools of Nursing,* offered only during Year Two, provided eight instructional hours per student to 569 nursing students. Table 1 details the number of students attending each program.

TABLE 1
Three-Year Summary of Student Attendance

Program	Fiscal Year 1	Fiscal Year 2	Fiscal Year 3	Three Year Total
Nursing Care of the Long-Term Patient	63	81	58	202
Refresher and Pre-Service (In-Service) Course for Social Workers	22	45	22	89
The Clergy and Rehabilitation of the Chronically Ill	45	40	29	114
Stroke in Your Family	380	520	362	1,262
Community Nursing Education	3,638	5,162	9,356	18,156
Regional Service to Schools of Nursing	—	569	—	569
Total	4,148	6,417	9,827	20,392

The regional impact of the program has been outstanding with all sections of the state represented by participants. Out of 87 counties in Minnesota, health related professionals from 77 counties, or 88.5%, attended these programs. Only Big Stone, Clearwater, Grant, Kanabec, Lake of the Woods, Mahnomen, Murray, Red Lake, Traverse and Wabasha counties were not represented. The community and/or family stroke education seminars were presented in 70 Minnesota counties. Table 2 indicates the geographical distribution of the students at the Kenny Institute based courses.

TABLE 2
Geographic Distribution of Kenny Students

Georgraphic Area	Year 1 No.	Year 1 % age	Year 2 No.	Year 2 % age	Year 3 No.	Year 3 % age	Total No.	Total % age
Twin Cities	64	49.2	80	48.1	51	46.8	195	48.1
Out State	51	39.2	56	33.7	42	38.5	149	36.8
Out of State	15	11.6	30	18.2	16	14.7	61	15.1
Total	130	100.0	166	100.0	109	100.0	405	100.0

In 1970, approximately 46.7% of Minnesota's population lived in the Twin Cities metropolitan area. It should be noted that a comparable ratio, or nearly half of the students, attending the in-depth longer courses were from the Twin Cities area with the percentage decreasing slightly from Year One to Year Three. Out-state representation was lower during Year Two but averaged approximately 39% for the other two years.

Finally, an additional increase in the numbers of those providing improved stroke care resulted from the return of *Social Work Refresher* students to medical employment after attending the course. Of the 89 students in the *Refresher and Pre-Service (In-Service) Course for Social Workers,* 35 were refresher students. Twenty-four (68.6%) of these 35 students returned to positions in the medical field, two became ill and could not seek employment, four are not yet available for employment and five could not be reached for follow-up.

Project Objective 2

To upgrade the technical skills and knowledge of health related professionals regarding stroke

and rehabilitation, emphasizing the broadened scope of activity possible in traditional professional roles.

With the assistance of both educational and clinical experts, the curricula of the courses on *Nursing Care of the Long-Term Patient, Social Work Refresher and In-Service Course* and *The Clergy and Rehabilitation of the Chronically Ill* were all designed to meet the goal of upgrading technical skills and knowledge. In addition, the students were tested as to information and clinical skills learned, follow-up questionnaires were developed and on-site evaluations of student performance were conducted.

In the *Nursing Care* course the students were given a pre and post test of 48 questions. Test results indicated that prior to the course only half of the students could answer 70% of the questions successfully, whereas after attending the course all of the students could answer at least 73% of the questions. A low correlation ration of .355 between the tests showed a definite but small relationship indicating that scores on the post-test were only slightly influenced by pre-test results. We may, therefore, conclude that the students' knowledge of rehabilitation nursing increased as a result of course participation.

Six-month follow-up questionnaires to the nurses revealed that a majority of the students were still employed at the same institution. Student on-the-job changes related to course attendance were: (1) in-service training of staff in rehabilitation methods and techniques of nursing care learned at the course; (2) implementing an improved concept of rehabilitation by teaching patients new skills and encouraging greater patient independence; (3) practicing and teaching more effective means of communication between patients and staff; and (4) purchasing and modifying equipment for proper usage.

Site evaluations were conducted with 92 former students. Most considered the course to have been "excellent," "worthwhile," "helpful" and "pertinent." Moreover, each participant mentioned gaining insight from whatever portion of the course was applicable to her particular situation. New techniques and equipment were cited as presently being used regularly, and staff development programs had frequently been initiated.

Negative reaction was mostly related to expressed desire for a longer course with additional time available for clinical practice. Difficulty in implementing new methodology at the employing institution was also mentioned.

Students in *The Clergy and Rehabilitation of the Chronically Ill* were given a pre and post test of 20 situational, multiple choice questions. Only half of the students tested could answer 71.03% of the questions correctly before attending the course. After course participation, 82.4% of the students scored 15 (75% correct) or better. Inasmuch as the mean scores (pre: 14.206 and post: 16.5) were significantly different at the .001 level, we may conclude that course attendance significantly raised the students' level of knowledge regarding rehabilitation and chronic illness.

A follow-up questionnaire was developed to ascertain the students' evaluation of the material covered in the course. Thirty-four students (68% of those contacted) responded, and all regarded the course as contributing positively toward their effectiveness in ministering to the chronically ill. In regard to the amount of time allotted to various areas of knowledge, over 50% of the students indicated they would have preferred more information on the psychosocial aspects of disability and 32.4% requested more discussion of the relationship between the physician and the clergyman. Coverage of medical aspects of disability was judged excellent by 70.6% of the clergy.

Behavioral objectives were delineated for all content areas covered in the *Refresher and In-Service Course for Social Workers.* Students were asked to evaluate content areas as to significance and meaning for them. Those topics rated as excellent in organization and coverage were "Behavior and Learning Difficulties in Children," "The Meaning of Stroke," "Psychology of Death and Survival," "Community Resources for Crisis Intervention" and "New Directions in Health Careers." "Administration in Institutions Employing Social Workers" was considered least satisfactory. The students also rated the total course as outstanding in worth and of unusually high quality. Achieving the project goal to upgrade stroke skills and knowledge was further indicated by the 47 employed medical social workers who attended the course for in-service training purposes.

During the three years of the project, all Kenny course presentations were evaluated by the students as to organization/coverage and style/delivery. Comments were also requested regarding the overall character of the course. As a result

of these evaluations, appropriate changes were made in speakers, topic focus or other aspects of the course format.

Project Objective 3

To facilitate the development of dialogue and inter-institutional cooperation throughout the state.

In order to achieve this goal, each project unit involved health professionals from throughout the state in curriculum planning and course instruction. Where possible, former students were contacted and included in planning, teaching or evaluation capacities. The total group represented the full range of health disciplines and presented a unique opportunity for increased understanding and dialogue among these persons and the student professionals. Of a total 457 classes conducted for these courses, 79 (17.3%) were taught by University of Minnesota faculty including 34 from the Medical School, 28 from the School of Social Work and 17 from other departments. Instruction for 239 (52.3%) classes was provided by hospital personnel, specifically doctors, nurses, physical and occupational therapists, social workers, psychologists and speech pathologists. Although the majority of these hospital personnel were from the Twin Cities area, 21 (9%) were located outstate. 68 (14.9%) instructors were from social welfare agencies, and 28 (6.1%) were physicians in private practice.

Project Objective 4

To increase knowledge and understanding of the regional lay public, especially the families of stroke patients, regarding stroke.

Stroke in Your Family, as a vehicle for educating patients and their families, reached 1,262 participants from 18 Minnesota counties. Approximately half of these students were family members, and half were local health professionals. As mentioned earlier, community health professionals were regularly included in course planning and instruction.

At the conclusion of the course, *Stroke in Your Family* participants were asked to complete evaluation questionnaires describing the status of their stroke patient, what information received would help them to improve the patient's care and how this information would help. Although nearly every point of information was mentioned as helpful by someone, the suggestions considered most valuable related to patient self-help, individualized household equipment and utensils, patient exercise, techniques for moving and lifting, and explanation of patient attitudes. Participants felt the information given would enable them to help the patient be more comfortable, improve his attitude, make communication easier and contribute to a better understanding of the patient's problems. Repeatedly, the participants rated the presentations as excellent, informative, interesting and practical.

Conclusion

This project was originally designed as a statewide program of continuing education, and the pattern of student attendance indeed denotes an outstanding regional impact. Although nearly half of Minnesota's population lives in the Twin Cities metropolitan area, only 25.9% of the total student enrollment was from that section. Participation from outstate health professionals and laymen was therefore proportionately greater than might be anticipated. Of the 11 economic regions so designated by Northlands Regional Medical Program, those in the Central, North Central, and South Central portions of the state are represented more heavily than their ratio of the total state population would predict. However, the North, West and West Central regions were represented somewhat less frequently than their population ratio might indicate.

Overall, it may be concluded that the project goal has been realized of developing within local communities multidisciplinary clusters of stroke-sophisticated health professionals and laymen. With the encouragement and support of the project educators, many of these individuals are now able to conduct inservice training, family education and community programs on stroke, as well as to provide high quality medical care to stroke victims.

Obviously the need for such educational programs is evident, and health professionals throughout the state are eager to take advantage of opportunities to improve their patient care capabilities. Unfortunately, this project, with its diverse emphasis on centralized indepth courses as well as decentralized, outreach programs, cannot be integrated into any presently available educational structure. Highly specialized faculty are necessary to teach in the courses for rehabilitation nurses, the clergy and social workers; and the state technical, junior college and four-year schools

do not have sufficient qualified staff available. It is, therefore, advisable for future efforts and funding to be directed toward development of educational materials packages (audiovisuals, student handbooks and instructor guides) that will enable relatively unspecialized personnel in concerned communities and facilities to offer similar courses.

Summary

As a component project of Northlands Regional Medical Program, the Sister Kenny Institute, Minneapolis, developed a three-year integrated plan of continuing education on stroke rehabilitation and chronic illness. This program provided short courses for nurses, social workers, clergymen and families of stroke patients. In addition to increasing the number of stroke-sophisticated professionals and laymen, it has also been a project goal to encourage health professionals to incorporate new skills and knowledge into their own institutional programs or to replicate some courses in their own communities. By these means, it has been possible to multiply the effects of the project and help maximize the physician's efforts to provide improved patient care.

Improving Allied Health Capability Through Continuing Education

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THE HEALTH CARE SYSTEM of the United States is at a point where any planned improvement in the quality of the services available must take into greater account certain non-medical factors. A very significant consideration is that of economics. Historically, the phrase "cost benefit ratio" has been an active part of the daily vocabulary of engineers and accountants but was not even included in the glossaries of the standard works for the health care specialties. Although there is general awareness of this spiralling cost among the nation's 3½ million allied health personnel, there is little anlytical understanding of its causes. If forced to consider basics, a significant majority would point to the familiar whipping boy "inflation" as the single most significant contributing factor and might cite the wider utilization of allied health workers as being another. They would probably state, and find general agreement, that whereas inflation adds to the cost but not to the quality of health care, at least the expenses entailed in broader use of allied health specialists bring a proportionate increase in the quality of care afforded the patient. That is a comforting thought, but is it rational?

One inescapable fact is that even with improved health as the object, there is a ceiling on the willingness and the ability of either the individual or the nation to continue to meet escalating costs. Any attempt to raise standards of quality while holding the line on costs must acknowledge that, although the inflationary spiral is beyond early control, the manner in which the various allied health specialists are utilized should be very much within the control of the health industry. Considering that personnel costs account for more than a solid 50 percent of hospital budgets, more efficient use of each member of the allied health team is a logical starting point in a program to improve the cost benefits ratio as applied to health care.

The program described in this paper is a joint effort of health professionals with the support of the Northlands Regional Medical Program, Inc., to work toward a partial solution in one allied health area. The project was designed to conserve manpower already trained and to upgrade the skills and level of performance of members of one health specialty—dietetics.

Manpower Needs

Historically, allied health workers fit into tight categories, with very little overlap of responsibility and with no progression, either between groups or upward, except within structured specialty groups. "Professionalism" of the allied health science specialties has been advanced and maintained by national associations which set educational standards for the specialty, and by licensure, registration, or accreditation where these apply to individual practitioners.[1] The American Medical Association, through its Council on Medical Education, is represented on boards that accredit education and training programs for 13 allied health professions. While it is true that such "professionalism" has been instrumental in setting and maintaining standards of preparation and (perhaps) performance, the rigid structure and lack of flexibility which result have had less desirable effects.

The wide use of health care professionals is defensible and desirable when improvements in patient care result and when total availability of health care is extended. Unfortunately, during the recent period of rapid change, no close administra-

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tive scrutiny of scope and responsibility of each health specialty or analysis of job performance was attempted for allied health manpower. Accredited programs of preparation were equated with permanent competence, although costs can only be justified by continuing levels of excellent performance.

In the recent past, the chief area of interest in health manpower has been in the direction of increasing numbers. Both federal support and academic programs have been designed to facilitate production of manpower. Unequal attention was given during this period to the continuing education of specialists and to the revision of training programs in the light of present and future needs for particular *types* of personnel. Instead of reassessing traditional programs to promote flexibility and reducing patient care costs by utilizing specialists at their highest technical level, new specialties were introduced and approved through organization of new professional groups. Examples of these programs are the various technician specialists, the physician assistant, etc.

Dietitians are among the allied health workers to whom the observations above apply. The American Dietetic Association is the national profcssional organizaion which sets educational standards for undergraduate programs in dietetics, approves internships in dietetics, and sets requirements for registration of dietitians. It also grants approval for programs of continuing education to meet standards for maintaining registration.

Assessment of Regional Needs

Information on the subjective need for continuing education and the probable response of dietitians was obtained from a survey. With the cooperation of the Minnesota Dietetic Association, all persons working as "dietitians" in Minnesota were surveyed in 1968.[2] The questionnaire and the tabulation of the results were developed by the staff of the American Rehabilitation Foundation of Minneapolis. The Dietetic Association provided lists of American Dietetic Association members, non-ADA dietitians and consulting dietitians. In the course of the survey, respondents submitted names of other individuals who were working or had worked as dietitians. In total, 635 questionnaires were mailed; 419 (66%) were completed and returned. Of the 419 respondents, 277 (66%) were currently employed as dietitians; 162 (38%) full time; 79 (19%) part time; and 36 (9%) consultants did not indicate either full or part time. The 152 inactive dietitians (34%) who responded included: 29 (7% of 419) employed in other fields; 101 (24%) not employed; and 12 (3%) retired.

Three-fourths (319 or 76%) of those who responded to the survey indicated an interest in refresher training: 266 (63%) at the graduate level; and 53 (13%) at the undergraduate level. Of these 319, 231 currently were employed as dietitians and 88 were inactive; this represents 89% of the active dietitians and 65% of the inactive dietitians. Of the 101 inactive dietitians, 50% expected to return to employment.

Goals of Continuing Education in Health Specialties

In 1969, a vote of the membership of the American Dietetic Association approved registration based on a requirement for continuing education. Dietitians are among the very few health groups accepting mandatory education as a prerequisite to continuing registration.

Three factors operate to make educational programs in clinical nutrition a valuable state and national asset in dietetics.

First, the cost of dietetic internships, which is supported by hospital administration (and is therefore a part of patient cost) is becoming prohibitive. Dietetic internship availability is declining. Students fully qualified by undergraduate training cannot be placed in internships. In this situation, the undergraduate enrollment in dietetics is certain to decrease. Actual numbers of registered dietitians, trained in approved undergraduate programs *and* in approved internships will not meet the anticipated health care needs of the future. It is therefore important to conserve and use trained manpower, at least until opportunities for completion of dietetic training again become more available.

Second, it is the usual situation among allied health workers (largely women) that professional activity is often interrupted by marriage and family responsibility. Studies have shown that retraining programs have been successful in returning allied health specialists to active work.

National studies have shown that the number of nurses who return to active duty varies between 50-70% after refresher training.[3] Followup studies on Minnesota nurses who completed refresher training have been done by the American Rehabilitation Foundation. Questionnaires were sent to

279 nurses who had completed refresher training between 1960-66. One hundred and thirty (69%) of the 188 responding to the questionnaire had returned to work at some time after the course.

Refresher courses in other allied health areas have also been conducted by the American Rehabilitation Foundation with the aid of Community Health Services grants. Followup studies on those retrained in 1967 and 1968 gave the following results:

Specialty	Number Retrained	Number Reactivated	Percent
Occupational Therapists	17	14	82
Physiotherapists	23	20	80
Social Workers	33	33	100

It is difficult to obtain figures on return to work for clinical dietitians following refresher courses because formal courses of this type are not widely available in the United States, but it may be assumed that the pattern would be similar to other health workers groups' experiences.

Third, if the full utilization of already trained dietitians is a primary goal, it is imperative to provide for updating of knowledge and skill. The rapid advance in medical knowledge has major impact in the practice of clinical nutrition. New information and new techniques must be made available to all dietitians, both those in retraining programs and those currently employed. In addition, this type of education must be made available on a wide geographic basis, not only in the educational and medical centers of the area.

It is also vital to upgrade the skills of those persons functioning in the nutritional care of patients but who have had very little formal dietetic training. They are often the only community resource in nutrition.

Future Needs

Another important consideration in structuring education programs is the forward look required to identify needs of the future. Admittedly, it is difficult to predict skills requirements of the future, but certain information is available. The shift of patient load from acute care to continuing care beds is obvious.[4]

The interest in nutrition as an element of preventive medicine is also emerging, as is the new understanding that nutrition education is a necessary part of care for the disadvantaged of any type, as well as for the person suffering from a chronic condition requiring diet therapy.

Number of Beds in Minnesota Licensed Medical Facilities

Facility	1943	1971	Percent of Increase
General Hospitals	11,159	18,996	70%
Nursing and Boarding Care Homes	3,905	41,313	958%

In the light of the factors described above, a program of Continuing Education in Clinical Nutrition was designed and submitted to the Northlands Regional Medical Program, Inc. The program was approved and funded for a two-year period. It was operational from March 31, 1970, to March 31, 1972. The major goal of the project was the improvement of patient care through an increase in dietetic competence and availability.

Design of the Program

This Minnesota-Northlands Regional Medical plan was designed, in part, to increase the number of dietitians available for service in this allied health specialty by re-educating the once fully trained, but now inactive, dietitian in order to facilitate her return to employment. The group of inactive dietitians had been identified by the survey. Approximately 50 percent expected to return to work and 65 percent of the group requested programs of continuing education.

In order to increase dietetic availability, this program was also designed to meet the needs of "consulting dietitions" in Minnesota. These persons were working full or part-time, and many were employed by a number of institutions. Approximately 50 percent of this group had never been trained in clinical dietetics but were "consultants" to institutions engaged in patient care. These consultants were also identified individually by the survey.

A third group for which this program was planned was the isolated dietitians in the state who have very little opportunity to participate in programs of continuing education. Availability of competent clinical nutritionists throughout Minnesota depends in great measure on a program of modern diet therapy for this group.

An educational program of current information in nutrition and diet therapy for these three groups was designed to meet their most pressing needs and to overcome the most limiting deficiencies in

TABLE 1
Continuing Education in Clinical Nutrition
One-Day Programs

Date	Place	Subject	No. Attending
November 2, 1970	University of Minnesota	Diet Therapy in Renal Disease	140
June 18, 1971	Minneapolis, Minnesota	Diet Therapy in Renal Disease	165
October 22, 1970	Mankato, Minnesota	Diet Therapy in Cardiovascular Disease	41
November 5, 1970	Moorhead, Minnesota	" " "	49
December 9, 1970	Minneapolis - DEC	" " "	50
December 15, 1970	Minneapolis - DEC	" " "	48
February 18, 1971	St. Cloud, Minnesota	" " "	47
March 16, 1971	Rochester, Minnesota	" " "	51
March 30, 1971	Minneapolis, Minnesota	" " "	45
April 22, 1971	Duluth, Minnesota	" " "	60
May 13, 1971	Minneapolis, Minnesota	Postgraduate Course in Diabetes Mellitus	114
October 28, 1971	Duluth, Minnesota	Management of Diabetes Mellitus	61
November 3, 1971	Morris, Minnesota	Symposium on Diabetes Mellitus	150
November 4, 1971	Minneapolis, Minnesota	Mgmt. of Patient in Nursing Home	33
November 11, 1971	Minneapolis, Minnesota	Current Concepts of Treatment and Research in Diabetes	57
December 3, 1971	Minneapolis, Minnesota	Parameters of Aging	55
December 10, 1971	Minneapolis, Minnesota	Seminar on Patient Education	74
December 11, 1971	Wadena, Minnesota	Coronary Care Seminar	120
January 21, 1972	Minneapolis, Minnesota	Nutrition and the Geriatric Patient	50
January 28, 1972	Minneapolis, Minnesota	Parameters of Aging	67
February 3, 1972	Minneapolis, Minnesota	Mgmt. of Patient in Nursing Home	40
February 28, 1972	Minneapolis, Minnesota	How Do People Learn?	53

TABLE 2
Continuing Education in Clinical Nutrition
Five-Day Courses

Date	Place	Subject	No. Attending
Nov. 16-20, 1970	Minneapolis - DEC	Current Concepts of Diet Therapy	10
December 7-11, 1970	Minneapolis - DEC	Current Concepts of Diet Therapy	7
June 14-18, 1971	Univ. of Minnesota	Current Concepts of Diet Therapy	35
March 22-26, 1971	Univ. of Minnesota	Current Concepts of Human Nutrition	20
May 17-21, 1971	St. Joseph, Minnesota College of St. Benedict	Current Concepts of Human Nutrition	9
Oct. 18, 19, 20, 1971	Concordia College, Moorhead, Minnesota	Current Concepts of Human Nutrition	6
October 12-16, 1970	Minneapolis - DEC	Clinical Experience as a Medical Team Member	1
October 26-30, 1970	"	"	1
November 9-13, 1970	"	"	1
Nov. 30-Dec. 4, 1970	"	"	4
Dec. 28-31, 1970	"	"	2
January 25-20, 1971	"	"	1
February 8-12, 1971	"	"	2
March 8-12, 1971	"	"	3
April 5-9, 1971	"	"	1
April 19-23, 1971	"	"	2
September 27, 1971	"	"	1
November 8, 1971	"	"	1
December 6, 1971	"	"	1
December 26, 1971	"	"	2
January 14, 1972	"	"	1

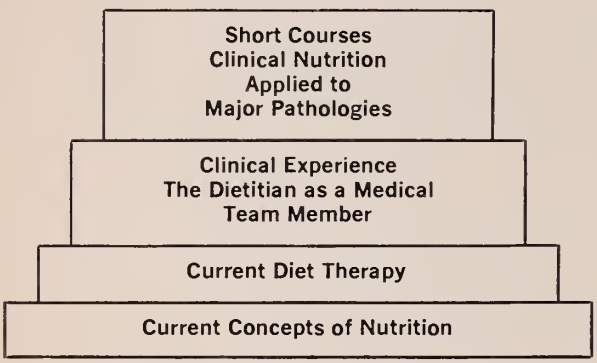
TABLE 3

Question:	Yes	No	% YES
Did you consider information received from this program valuable?	266	1	
Did the information supplement previous learning and experience?	266	1	
Were you employed at the start of the program?*	174	43	65
Have your professional responsibilities expanded* in the last year?	90	109	33
Are you currently employed (Part time, full time, consulting) Total	205		77

*Not every question answered by every respondent.

their preparation for employment as dietitians. The program of training or retraining was presented in three units of five days each. It was designed to present continuity of instruction with increasing levels of complexity.

The design also included a statewide short course program for all dietitians in Minnesota with the aim of improving competence and, therefore, increasing total availability of dietetic care.



Pyramidal Structure of Educational Units

Results of the Program

The response of dietitians to the courses was very gratifying. In Year 1, 909 persons participated in 8,820 hours of instruction. This response was far beyond the predicted participation, which was estimated at 155. The courses offered, their locations, and the attendance are compiled in Tables 1 and 2.

Response in Year II was equally satisfying. In the second year, 937 persons participated in 6,030 hours of instruction. The emphasis in the second year was directed toward the statewide one day short courses. This change in emphasis was implemented in response to requests expressed by registrants in Year 1.

Since the 1972 *total* membership of the Minnesota Dietetic Association is 603, it is obvious that many persons attended several education courses. One-day programs were open to all who have responsibility for nutritional support of patients, and a proportionally small number of nurses, social workers, physicians, etc. also benefited.

During the two year program, personnel from more than 200 separate institutions or agencies in Minnesota were registered for the courses.

Evaluation

Evaluation of the five-day courses was designed to test objectively the increase of knowledge for participants. This was accomplished by a program of pre and post testing, and a satisfactory increase in information was demonstrated. For 52 students enrolled in separate five-day courses in diet therapy, the average pre score on a 150 point test was 101.82. The average post test score was 117.54.

For 35 students enrolled in five day courses in normal nutrition, the average pre test score of a 150 point test was 117.29. The average post test score was 140.15.

One-day short courses were evaluated subjectively by participants. This response was overwhelmingly favorable, and comments and requests by registrants were used in the design of courses in Year 2.

On August 17, 1971, following a full year of operation, all Minnesota dietitians were surveyed to obtain information on benefits derived from this program. The number of questionnaires mailed was 685. The numbers returned was 267, a 38.9 percent response.

Pertinent information concerning total project evaluation obtained from this survey is listed in Table 3.

In June of 1972, all members (603) of the Minnesota Dietetic Association were questioned concerning employment status. There were 422 (70%) answers to the questionnaire returned. Of the 422 respondents 314 (74%) are employed, full or part-time, while 86 (20%) are not working. Of the 422 responses, 22 (5%) did not answer this question.

In contrast to the questionnaire of 1968, the percentage of inactive dietitians has decreased from 34% to 20% during a difficult economic period. It is, of course, impossible to measure the effect of this program in relation to the various economic factors operating during this period, but the increase in utilization of already trained manpower is significant.

Summary

In order to facilitate maximum use of dietetic manpower in the State of Minnesota, a two-year program of Continuing Education in Clinical Nutrition was designed. The objective of the proposal was to retrain inactive dietitians, and to offer current information on practice in clinical nutrition to

all persons with responsibility for the nutritional care of patients. The primary goal was to improve patient care by increasing dietetic availability and expertise. Response to the program was far beyond predictions. Maintaining official registration of dietitians was facilitated by the instruction, and non-dietitians were helped to overcome deficiencies of formal preparation in clinical nutrition.

Hopefully, some benefits derive from this program in the direction of controlling costs of patient care by improving performance of one group of allied health professionals through continuing education.

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Refresher and Continuing Education in Nursing

A New Role for Minnesota's State Junior Colleges

MARY M. MERGENS, R.N.

The Registered Nurse (R.N.) Refresher and Continuing Education project represents a unique cooperative effort between Northlands Regional Medical Program (NRMP) and Minnesota's State Junior Colleges. Through this association, it is now possible to conduct a four-week R.N. Refresher course or a two to three day continuing education workshop any place in Minnesota where (1) there is a need for such a program and (2) there are enough participants to make a program feasible.

This alliance between NRMP and the Junior College System holds tremendous potential for those concerned with health education and continuing education for health professionals.

The Need for a Coordinated Refresher Program

For years the critical shortage of nurse manpower prompted nationwide efforts to return inactive nurses to the work force. R.N. Refresher courses varying in length and quality have been offered in Minnesota since 1960. Refresher programs have been treated each year as a new problem and have been offered sporadically with little attention to state-wide planning and coordination. Courses were offered by private hospitals until 1965 when the Manpower Development and Training Act of 1962 was amended to include health occupations. Careful planning and coordination in these programs was often difficult however, because of the way funds were released. Often there was insufficient time for instructors to prepare lectures, arrange clinical facilities, order instructional materials and arrange guest lecturers. Recruitment of enrollees was a serious problem, because the MDTA courses required that the nurses be employed before enrolling in the course or that they commit themselves to working for the hospital sponsoring the course. Furthermore, these programs did not take into consideration the degree of insecurity which was so characteristic of students.

In order to correct some of these deficiencies, NRMP funded the original R.N. Refresher Proposal* which initiated a plan to incorporate R.N. Refresher courses into the State Junior College System in order to provide an on-going regional program throughout Minnesota. This program is particularly exciting because, to our knowledge, refresher education is not an on-going program or part of an educational system anywhere else in the United States. Many state nursing associations have inquired about the Minnesota program and have indicated plans to use it as a model in their own states.

The Need for Continuing Education Programs

Although the overall goal of the original R.N. Refresher project was primarily a manpower one —that of upgrading and regionalizing R.N. Refresher training in Minnesota in order to return inactive nurses to the work force—the process of developing and operating the Refresher Project uncovered many unmet and evolving needs among *practicing* nurses in health care facilities throughout the state. In every area where a refresher course was held during the past two years, employed nurses from local hospitals, nursing homes, public health agencies, schools and industries requested permission to attend many of the classes offered as "refresher" education to inactive nurses.

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*The original proposal was jointly prepared and submitted to NRMP by Ruth P. Stryker, then Director of Nursing Education and Publications at Sister Kenny Institute, and the Minnesota State Junior Colleges.

These practicing nurses were finding themselves ill-prepared, insecure and unwilling to accept the new ways in which they were being utilized in the expanding health care systems. Better utilization requires knowledge of new roles and the ability to perform them. During this final year of NRMP funding, the Refresher Project is attempting to adapt its curriculum to meet the educational needs of *practicing,* as well as *non-practicing* nurses.

This shift in emphasis, from refresher to continuing education has encouraged the development of several short-term in-depth programs which are being offered through the Community Service Departments of the Junior Colleges where refresher courses have been offered previously. Communication channels in these areas are fairly well established and local health care institutions have readily accepted and promoted these programs among their employees. Requests have been received from several institutions and individuals who have specified educational needs in the following areas: chemical dependency, pharmacology, geriatrics, nursing care plans, inhalation therapy, rehabilitation nursing, death and the grieving process and teaching and assessment techniques.

These requests reflect the major role which Nursing has come to play in all aspects of health care. As the nation's largest health service profession, Nursing must keep pace with new scientific and technological developments and with the expansion of programs and facilities in order to ensure effective delivery of health care. Nurses are taking on growing responsibilities in family counseling, screening for health problems, setting up community facilities and providing medical services. These expanded roles demand that nurses enter the profession with better preparation and new skills, and that they maintain their knowledge and skill at a level compatible with current practice.

Nursing, like medicine, and the other health care professions, is undergoing unparalleled change. The basic problem lies in finding ways of keeping pace with the increased demands for health care and all the advances in medical and scientific research which foster improved patient care. The growing demand for continuing education programs of all types and the accelerated development of such programs provide supportive evidence that continuing education is acknowledged by both consumers and providers to be one avenue of hope in keeping pace with professional progress. The specific objectives of the R.N. Refresher and Continuing Education project are:

A. To provide an on-going educational vehicle by which inactive nurses can return to their profession, thereby improving the qualitative maldistribution of nursing care in Minnesota.
B. To perfect the Junior College mechanism of offering the refresher courses with maximum effectiveness and efficiency.
C. To adapt certain components of the current refresher curriculum to meeting the needs of employed nurses who are facing expanding demands in their professional roles.
D. To establish within the Junior College System a "clearing house" or resource center of information where individuals or institutions can obtain referrals to the appropriate people, places and programs which will help them to update and increase their knowledge and skills in health care.

Methods

The four-week nurse refresher course combines classroom content based on recall of previous learning and presentation of new information with clinical experience in local hospitals or other health care facilities. It is felt that anything less than 120 hours of instruction does not meet the educational needs of the inactive nurse. The courses are planned with six hour days, five days a week because continuity is lost if classes are stretched over many weeks. Most nurses can plan for an educational program best if it is concentrated for a single month.

Eligibility requirements for the course are very broad so as to provide any interested nurse the

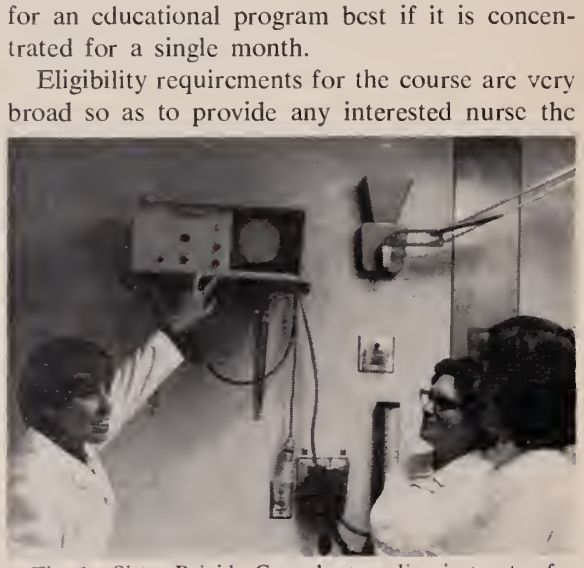


Fig. 1—Sister Brigida Cassady, traveling instructor for the Project demonstrates cardiac monitoring equipment for two nurses enrolled in the refresher course at Metropolitan State Junior College in Minneapolis.

opportunity to update her knowledge. All nurses taking the refresher course must have a current Minnesota license or be in the process of obtaining current licensure.

The course curriculum devotes special attention to the nurse's expanded role in the delivery of health care by including information on teaching and learning, creativity, effective communication, death and grieving, drug abuse, coronary care and much more (See Figures 1 and 2).

The emphasis is on *nursing care* rather than the setting where it is practiced. Another major emphasis is to utilize local health care facilities and resource people in the communities where courses are offered. This principle of participation was designed to make the inactive nurse aware of local health resources and work opportunities.

As sponsoring agent for the project the Junior Colleges provide classroom space, audiovisual equipment, registrar services, and assistance with student recruitment and course publicity. News releases, radio and T.V. spot announcements, college bulletins, descriptive brochures and individual mailings have all proved very effective means of publicity and recruitment.

Instructors for the course must have a minimum of a bachelor's degree and two years of teaching experience. Most have Master's level preparation and are recruited from the area where the course is to be offered. Where library facilities are unavailable and there are no qualified instructors, a traveling library and instructors are provided. Clinical experiences are provided through local health care facilities. Inservice or supervisory personnel assist students with patient care while the instructors prepare assignments and goals for each day's experience.

Per diem stipends are made available to students who must travel outside their own vicinity to attend a course.

It is anticipated that the refresher program will become a permanent component of the Community Service Programs of the Minnesota State Junior Colleges when the three-year affiliation with NRMP expires in March of 1973. This provision to phase out NRMP support and establish an on-going regional program of refresher training in Minnesota was included in the original proposal. Plans are underway at this time to offer the R.N. Refresher Course for college credit (30 hours per week = four credits). These extension credits will make the program eligible for state support and will assist many RN's to earn educational salary increments.

The mechanism for offering the short-term continuing education workshops is much the same as that for the refresher courses. The junior colleges provide assistance with publicity, recruitment and physical arrangements including classroom, registration and fee collections. Workshop faculty are generally guest lecturers who receive honorariums for their services.

Since participation of local community health resources has been such an integral part of the program design, the project has compiled a valuable backlogue of the health resources available in each area where a course has been offered. As the program expands to all the Junior college locations (See Figure 3), the Project will have established working relationships with most of the people and organizations who could help nurses update their knowledge and skills in health care.

This wealth of resource information will be regionally categorized and may eventually provide the foundations of a "clearing house" or resouree center of information. A center such as this which could be readily utilized by individual practitioners, schools of nursing, hospital and nursing home inservice personnel, will require coordination and cooperation of all of Minnesota's "providers" of continuing education.

Evaluation

The evaluation of this program includes both quantitative and qualitative aspects. The quantitative evaluation consists of the number of courses and workshops offered each year, the number of



Fig. 2—Nurses at the Willmar State Junior College course update their knowledge of inhalation therapy procedures through a demonstration and practice session at Community Memorial Hospital in Willmar.

nursing personnel attending each offering, the number of refreshers who return to active employment and the length of time they remain employed. This information is gathered by a follow-up of each refresher at the time of the course and at six month intervals.

The qualitative evaluation will include (1) evaluations of courses by instructors at the end of each offering; (2) evaluation of student performance at the end of each course; (3) evaluation of course by student at the end of the course and 6 months after the course; (4) evaluation of the overall program as it meets state-wide needs for more qualified personnel each year; and (5) evaluation of performance by the employer after three months of employment.

Results

During the first two years of the project, there have been 11 refresher courses with 314 students attending. (See Table 1). Eight of these courses were offered in the Twin Cities area and five in the outlying regions of the state. Approximately 56% of those nurses who responded have returned to active participation in the profession. Although the demand for refresher courses has been greater in the Twin Cities Metropolitan area, regionalization of the program remains a top priority in planning courses.

As a part of the ongoing quantitative evaluation of the project and in order to assess the effectiveness of the refresher courses, questionnaires were sent to the refreshers six months after they completed a course. The results of this initial follow-up survey appear in Table 2. It is interesting to note that although only 56% of those who responded were actually back to work, 65% of those who were not employed indicated their intention to return to the profession within the year. Only 23% of the respondents indicated that they would not return to nursing barring unforeseen circumstances. Most nurses who had not returned to work cited family circumstances as their reason for not returning.

At this time, a second phase of evaluation, that of the re-employed nurse by her employer, is being implemented. This evaluation of performance by the employer reveals the ultimate value of the course. If refreshees are working, the numbers and quality of their work are indeed the most important results of the course.

TABLE 1
RN Refresher Courses 1970-1972

Location	No. of Students Completing Course
Metropolitan State Junior College Minneapolis, Mn. (four courses here)	120
Metropolitan State Junior College St. Paul Campus	34
Willmar State Junior College Willmar, Mn.	8
Wadena Extension Division Wadena, Mn.	11
Rainy River State Junior College International Falls, Mn.	14
Brainerd State Junior College Brainerd, Mn.	14
Austin State Junior College Austin, Mn.	13
Anoka-Ramsey State Junior College Coon Rapids, Mn.	23
Normandale State Junior College Bloomington, Mn.	36
Lakewood & Inver Hills Junior Colleges White Bear Lake & Inver Grove Heights, Mn.	46
Total	319

TABLE 2
Follow-Up Six Months After Completion of R.N. Refresher Course*

Employment Status	Number & Percent of Nurses
Employed in Nursing	77 (56%)
Full-time	26 (34%)
Part-time	51 (66%)
Not Employed in Nursing	62 (44%)
Planning to return within one year	40 (65%)
Planning to return but time undetermined	8 (12%)
Enrolled in Higher Education Programs	0
Not planning to return	14 (23%)

*Number and percent of inactive registered nurses completing a refresher course according to employment status six months later.

TABLE 3
Continuing Education Workshops Offered in 1972

Location	Content	Attendance
Mesabi State Junior College Virginia, Mn.	Rehabilitation Nursing	87
Willmar State Junior College	Chemical Dependency Studies	30
Northland State Junior College Thief River Falls, Mn.	Quality in Nursing Care	59
Brainerd State Junior College Brainerd, Mn.	Quality in Nursing Care	12
	Total	188

Table 3 indicates the locations, content and attendance at the first four continuing education workshops offered through the project in 1972.

Discussion

The need to insure the establishment of an educational vehicle by which each new group of nurses can re-enter the work force annually has become increasingly apparent and there is substantial evidence to support the commitment of the Junior College System to this end. Each year the system has increased its financial support of this project's activities and has encouraged other nursing and allied health groups to plan continuing education projects within the junior college system. The R.N. Refresher and Continuing Education Project has with increasing frequency served as a liaison between representatives of a variety of health-related programs (i.e., long term care administration, Project Breakthrough, operating room nurses, community service personnel) and the Junior College Board.

The full potential of the State Junior College System for making continuing education offerings accessible to all health professionals has yet to be realized. As the present trend toward requiring proof of continuing education for relicensure continues to gain impetus among Minnesota's health professionals* the need for an education vehicle will become preponderant. The Junior College system has a well established network of educational facilities throughout Minnesota and has demonstrated enthusiasm and efficiency in implementing continuing education programs for nurses.

The recent report of the HEW Secretary's Committee to Study Extended Roles for Nurses† recommends that:

"Health education centers should undertake curricular innovations that demonstrate the physician-nurse team concept in the delivery of care in a variety of settings under conditions that provide optimum opportunity for both professions to seek the highest levels of competence. Financial support should be made available for programs of continuing nurse education that could prepare



Fig. 3—There are 18 state junior colleges in Minnesota. By 1973 there will be 20—including Riverview at Cambridge and Fairlakes at Fairmount.

the present pool of over one million active and inactive nurses to function in extended roles. The continuing education of nurses should be structured to encourage professional advancement among and through all nursing education programs and by encouraging the use of equivalency examinations to evaluate competence, knowledge and experience."

The potential of the R.N. Refresher and Continuing Education Project to implement this recommendation is enormous. The flexibility inherent in the program and the built-in capacity for frequent revisions, depending on the changing needs of nurses working at the community level, are two essential components of the project. In addition, the program promotes a growing recognition of the importance of physician-nurse collaboration in extending health care services to meet increasing demands. Many Minnesota physicians have participated in the refresher courses and workshops as guest lecturers and in planning clinical learning experiences. The students' written evaluations have reflected their appreciation of the physicians' class presentations, but more importantly, their realization that the medical profession in their own communities is interested and enthusiastic about their decisions to return to nursing.

Summary

A unique cooperative arrangement between

*Minnesota's State Board of Dentistry has already implemented such a proposal and resolutions on similar legislation were debated at the May, 1972 conventions of the Minnesota State Medical Association in Rochester and the American Nurses' Association in Detroit.

†Secretary's Committee to Study Extended Roles for Nurses. "Extending the Scope of Nursing Practice," JAMA, 220:9:1231, 1972.

NRMP and the Junior College System began in May, 1970, when Northlands funded a proposal to increase the number of professional nurses by a regional program of nurse refresher courses. Since that time 319 nurses have completed a refresher course and approximately 60% of these have returned to work. The success of the refresher project and the expressed needs of employed nurses for continuing education programs prompted Northlands and the Junior Colleges to expand their cooperative efforts to include the development of short-term in-depth continuing education workshops. These workshops are designed to help nurses keep pace with new scientific and technological developments and to prepare them for the new roles which are rapidly extending the scope of nursing practice.

As the pressures for a multi-professional approach to patient care have increased, and many Minnesota communities are struggling to coordinate health care facilities and resources with educational institutions, the RN Refresher and Continuing Education Project has cultivated productive and promising relationships with Minnesota's State Junior Colleges—relationships which hold much potential for future contributions to the professional growth of health practitioners.

Training Physicians and Nurses

for Intensive Coronary-Care Units

T. PAUL B. O'DONOVAN, M.B., B.Ch., JUDITH THIERER, R.N., HAROLD T. MANKIN, M.D. AND JOHN P. STOKES, M.D.

THE DEVELOPMENT of the concept of the intensive coronary-care unit (ICCU) is one of the major advances in medical cardiology in recent decades. When the procedure was implemented effectively, a gratifying reduction in in-hospital mortality from acute coronary heart disease was soon attained. In recognition of this, recommendations were made in 1964 at the Second Cardiovascular Conference to promote the ICCU concept nationally. In Minnesota, a special committee was formed to establish priorities for heart-disease control in our state. Members agreed upon five aspects of care in heart disease which should be given special effort, and their recommendations were accepted by the Minnesota Heart Association and the Heart Committee of the Minnesota State Medical Association. The first was implementation of the ICCU concept in our state. The Minnesota Heart Association (MHA) formed an ICCU Subcommittee for this purpose. A survey of coronary deaths in Minnesota for 1966 was undertaken to determine the magnitude of the problem. Major conclusions of this study were that a significant reduction in the hospital mortality rate could be achieved by furthering and advancing the application of the techniques required for the intensive coronary-care unit in hospitals throughout the state. Second, it was noted that there is an urgent need for responsible professional personnel to undergo appropriate orientation and training in the improved techniques of the aggressive management of acute myocardial infarction. Problems revealed by this survey included the following:

1. The number of nurses available was not sufficient for the staffs of future coronary-care units.

2. The current training of nurses did not provide adequate detail relating to coronary heart disease.

3. Medical directors were not generally available for supervision of coronary-care units and there was some reluctance on the part of physicians to assume this responsibility.

An ICCU planning grant was funded by Northlands Regional Medical Program (NRMP). The funds were to be used primarily for the training of physicians in the concepts of acute coronary care. Shortly after this planning grant was funded, NRMP requested the ICCU Committee to submit a full five-year operational grant to provide training programs in coronary care to meet the training needs of medical and allied health personnel. The primary objective of this operational project was to decrease further the death rate from coronary heart disease in Minnesota by means of multidisciplinary improvement in patient care. This was to be accomplished through the training of physicians, nurses, hospital administrators and medical electronic technicians in the modern concepts of coronary care.

The thrust of the project has been primarily educational and several approaches have been used.

Consultation Service

An on-site consultation service for the region was established with a corps of trained physicians and nurses, hospital administrators and medical electronic technicians as resource people. This service was designed to advise and assist hospital staffs and others interested in establishing coronary-care units and in problem-solving in existing units. Services included: planning and design of a coronary-care unit, proper choice of monitoring and other electronic equipment, advice regarding

Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

This demonstration project was sponsored by the Minnesota Heart Association, Minneapolis, Minnesota. It was a component of Northlands Regional Medical Program, Inc. supported by HEW grant #5 GO3 RM-00021. The opinions presented do not constitute endorsement by NRMP, Inc. or the Department of Health, Education and Welfare.

Judith Thierer is Director, Minnesota Heart Association-Northlands Regional Medical Program ICCU Course, Rochester Methodist Hospital, Rochester, Minnesota.

electrical safety procedures, development of guidelines and operating policies related to the electronic equipment and its maintenance. Approximately 128 of these on-site consultations have been provided throughout the state (Figure 1).

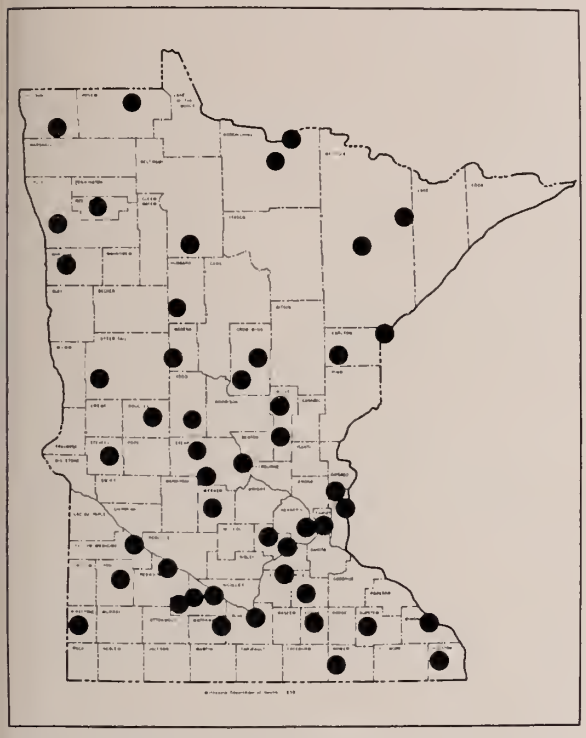


Fig. 1—Sites of on-site consultations, April 1, 1969, to March 31, 1972.

CORE Conference

A series of CORE conferences were held. These consisted of two-to-three-day intensive reviews of specific topics in acute coronary care, and were provided by the ICCU Committee with the assistance of an outside guest faculty. Table 1 lists these conferences, their location and the topics. The attendance at these conferences was generally limited to physicians actually directing or actively working in coronary-care units and their head nurses or their representatives. Two hundred eighty-five physicians and 78 nurses attended the eight conferences. Because the topics varied from conference to conference, many of the physicians and nurses were "repeaters," and attended several of these conferences.

The format of these conferences varied depending on the topic and the faculty. The most effective format which evolved was as follows: didactic presentations were made on specific topics and these were then followed by round-table discussions with one group leader and five or six of the participants. These periods were devoted to actual problem-solving with the use of information provided in the didactic presentations. When appropriate, actual demonstrations were given; for example, in the area of electrical hazards in coronary-care units. At some conferences, supervised experience in such technical skills as the insertion of a temporary transvenous cardiac pacemaker and the proper use of defibrillators and cardioverters was provided for the participants. It was felt that active participation by the physicians and nurses attending these conferences was the major ingredient in the success of this facet of the education activities.

Nursing Training and Refresher Courses

The advent of the coronary-care unit has provided a unique opportunity for the true multidisciplinary approach to the seriously ill patient. Increasing responsibility has been placed upon the nurse to the point at which she now has to make decisions and to initiate therapy in situations formerly reserved for the physician. Recognition of this fact is most important, for it can truly be said that the sine qua non of a successful, effective coronary-care unit is its corps of expert CCU nurses. Accordingly, a major objective of our project was to provide training in coronary care for those nurses already working in coronary-care units and for those who planned to work in units that were under construction or planned in the future. This was primarily accomplished through a formal ICCU nurses' course based at the Rochester Methodist Hospital in Rochester, Minnesota.

This facility comprises a full-size, fully equipped, two-bed mock ICCU, classroom facilities, office and storage space. It was completed

TABLE 1
ICCU CORE Conferences, Apr. 1, 1969, to Mar. 31, 1972

Location	Date	Title
St. Paul-Ramsey Hospital, St. Paul	April 1969	Coronary Care—1969
Rochester Methodist Hospital, Rochester	September 1969	Coronary Care—1969
Univ. of Minnesota, Minneapolis	February 1970	Arrhythmias and Sudden Death
St. Mary's Hospital, Duluth	July 1970	Coronary Care—1970
St. Paul-Ramsey Hospital, St. Paul	March 1971	Coronary Care—1971
Mayo Clinic, Rochester	June 1971	Coronary Care—1971
Miller-Dwan Hospital, Duluth	October 1971	Volts and Jolts—Electricity and the Heart
Univ. of Minnesota, Minneapolis	March 1972	The Failing Heart

in November, 1969, and the first formal course began on Nov. 17, 1969. This program is an intensive four-week course designed to prepare the nurse for her role as a highly skilled member of the coronary-care team.

The curriculum was organized to impart an advanced background in acute cardiovascular nursing. Areas of special emphasis include comprehensive coverage of the anatomy and physiology of the cardiovascular, respiratory, and renal systems; the epidemiology of coronary arterial disease and myocardial infarction; the pathophysiology of coronary arterial disease; fluid, electrolyte and acid-base balance; the medical and nursing management of the acute myocardial infarction and its complications; the nutritional needs of the cardiac patients; psychologic aspects of coronary-care nursing; electrocardiography with special emphasis on dysrhythmias; cardiac pacemakers; defibrillation and cardioversion; the pharmacology of cardiovascular drugs; external cardiopulmonary resuscitation; principles of pulmonary ventilation and support; the team concept of coronary-care nursing; the medicolegal aspects of coronary-care nursing; and coronary-care unit management.

Enrollment is limted to 12 nurses per course. Didactic presentations are augmented with audiovisual aids, small group-study sessions, experience in the simulated unit and clinical experience in the coronary-care units of Rochester Methodist Hospital and St. Marys Hospital. The director of the ICCU nursing course and her assistant are responsible for much of the instruction; members of the Departments of Cardiovascular Disease, Pathology and Electronic Engineering of the Mayo Clinic also serve as instructors. Opportunities for individual instructor-student conferences are provided. A most useful teaching tool has been replaying of videotape recordings of the students' performances. For example, a simulated resuscitation and defibrillation for cardiac arrest may be videotaped. Replay of the videotape and constructive criticism by the instructors and other members of the group have been invaluable in effectively teaching correct procedures and techniques.

To date 20 such courses have been held at the Rochester Methodist Hospital (RMH), with a total attendance of 232 nurses. Five similar courses were held under the auspices of the joint MHA-NRMP ICCU project at St. Joseph's Hospital in St. Paul. Figure 2 shows the geographic distribution of the attending nurses.

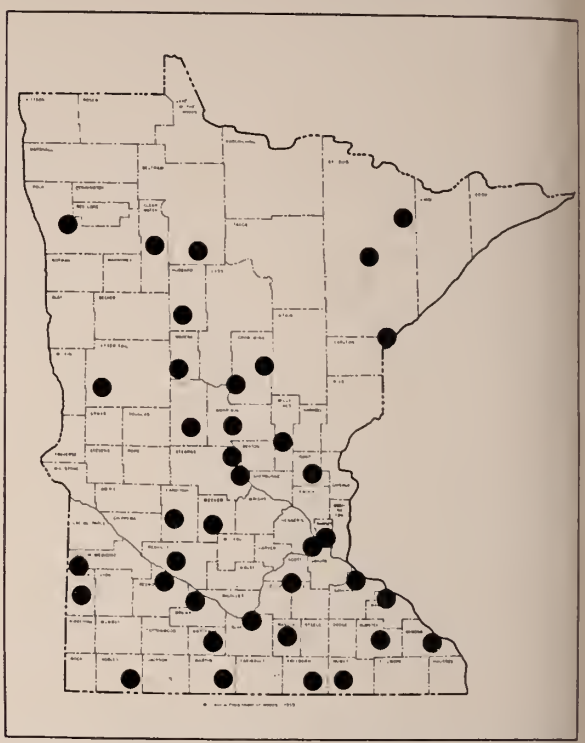


Fig. 2—Location of nurses attending the ICCU nursing course, April 1, 1969, to March 31, 1972.

For evaluation purposes, pre-tests and post-tests are given to each group attending the course at RMH. The mean pre-test score for the first 17 courses was 72.1% and the mean post-test score for the same period was 93.2%. A two-day refresher course is offered yearly to update knowledge and skills of graduates of this course. The four refresher courses have been attended by 187 nurses and have been highlighted by the presence of guest faculties from outside the area, as well as by leaders in coronary-care nursing in the state of Minnesota. For evaluation purposes, the pre-test and post-test were given again to the group attending the 1971 refresher course, and mean scores for this group were as follows: pre-test, 72.9%; post-test, 94%; and 87.1% on the refresher. Of the 54 participants in the retest at the refresher course, 45 showed an average loss of retention of seven percentage points, three had the same score and six increased an average of a little more than two percentage points. A small number of this group recently repeated the same test at the end of two years, and retention figures from this group will be available shortly.

Area Seminars

Fifteen area seminars within our region were held. These were designed as half-day to one-day courses, the subject matter being decided in consultation with the hospitals or physicians requesting the seminar. Eleven of these seminars were for physicians, nurses and hospital administrators and four were specifically for medical electronic technicians (MET). The location of these seminars is shown in Figure 3. The early seminars were aimed primarily at generating an interest in and concern for development of coronary-care units where none existed. Later, the seminars were devoted to recent advances in coronary care for the attending physicans and nurses. Table 2 lists the number and types of our educational programs and the attendance.

TABLE 2
Educational Programs and Attendance

Educational programs		Attendance MD*	RN*	ADM*	MET*
Total number of seminars					
Area	11	230	488	56	10
MET	4				108
Total number of CORE conferences	8	285	78		
Total number of nurse-training courses					
Rochester Methodist	20		232		
St. Joseph's	5		62		
Total number of nurse-refresher courses	4		187		

*MD = physician; RN = registered nurse; ADM = administrator; MET = medical electronic technician.

Dial Access Program

Eighteen fve- to six-minute pre-recorded presentations dealing with topics in the field of acute coronary care were prepared under the supervision of the ICCU committee. These were made available through the Dial Access Program of NRMP.

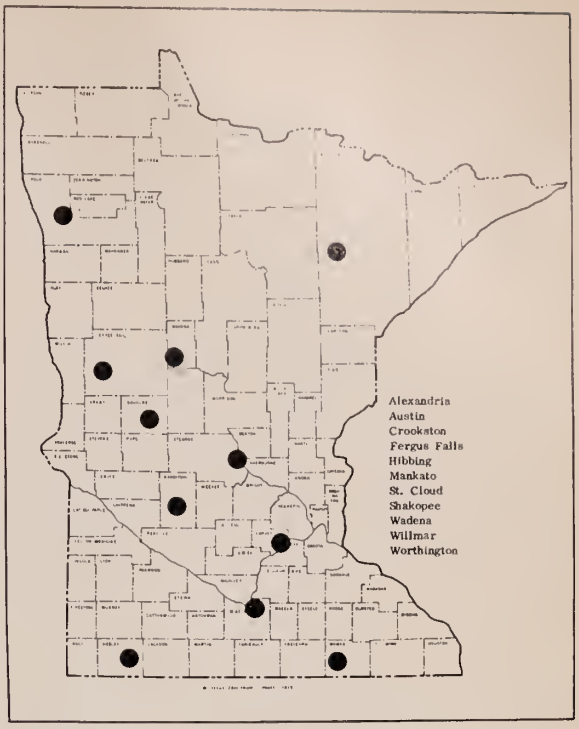


Fig. 3—Sites of area seminars, April 1, 1969, to March 31, 1972.

Coronary-Care Newsletter

A regular coronary-care newsletter was established under the editorship of Dr. John Morgan. It was mailed to professional personnel involved in coronary care throughout the state. This newsletter contained information on the joint MHA-NRMP ICCU project, as well as summaries and comments on recent articles in the cardiologic literature dealing with acute coronary care.

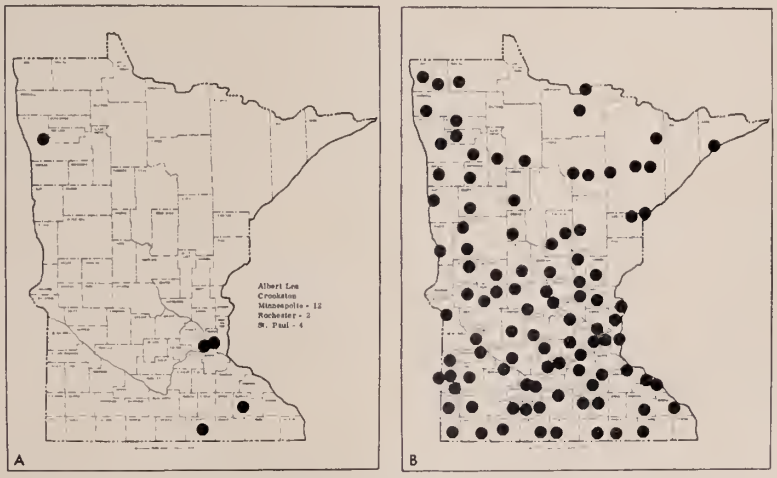


Fig. 4—*(A)* Number of ICCU's and MICU's (Medical Intensive Care Unit) in 1967. *(B)* ICCU's and MICU's in 1972.

Educational Materials

Educational materials were provided either permanently or on loan through the project. The average number of these mailed out annually has averaged 500. In addition to pamphlets and booklets, specific films were made available on loan, and mannequins for the teaching of cardiopulmonary resuscitation also were provided on loan.

Results

The results to date have been gratifying. Figure 4 shows that in 1967 there were 18 Minnesota hospitals with ICCU's, combined medical ICU-CCU's (MICU) or with portable monitoring equipment. By Mar. 31, 1972, 119 Minnesota hospitals had such facilities. Prior to the development of the ICCU concept, the average in-hospital mortality rate from acute myocardial infarction ranged between 30 and 35%. The Minnesota coronary-care mortality study of the ICCU project, now in its second year, has shown that the over-all mortality rate from acute myocardial infarction in Minnesota is now 22%. It is well known that most acute coronary deaths occur within the first few hours after the onset of an episode of ischemia. Thus, we have been gratified to find that the average time from onset of symptoms to arrival at the coronary-care unit has decreased from four and a half to three and a half hours in our most recent survey.

A one-year follow-up study showed that 77.8% of the nurse participants in the ICCU training course were working in coronary care at the time they attended the program. Many participants worked in medical or surgical intensive-care units, emergency rooms, cardiac postoperative surgical units and postanesthetic rooms, and they returned to these same areas after completion of the course. However, of the 77.8% actually working in coronary-care units, 91.4% were still engaged in coronary care at the end of one year. Equally impressive is the fact that 91.2% were still employed by their sponsoring agency at the end of one year. This figure is somewhat misleading in view of the fact that some hospitals do ask their nurses to stay for one year after taking the course.

Members of the ICCU project are pleased to note the improvement in the care of the patient with acute coronary disease in Minnesota. The aid of the Minnesota Heart Association and the Heart Committee of the Minnesota State Medical Association, for their sponsorship, and of Northlands Regional Medical Program, for its support and funding, has been crucial. We should like to express our appreciation to the dedicated present and past members of the ICCU project who have given so much of their time and effort to further this cause. We also owe much to the physicians, nurses, hospital administrators and electronic technicians of Minnesota who attended these educational programs and in turn improved coronary care in their area. Their unselfish support and cooperation have been largely responsible for the success of the project. The training of health professionals in acute coronary care in Minnesota has been truly a multidisciplinary team effort.

Continuing Education for Laboratory Personnel

in Small Rural Hospitals

BARBARA MERRITT, M.S., M.T. (ASCP)

RAPIDLY CHANGING technology in the health sciences has intensified the need for continuing education of all health care professionals. If competent on-the-job performance is to be maintained, personnel must be kept informed of new developments and continuing education programs must be relevant to work needs.

Availability of continuing education programs for laboratory personnel and other health professionals has increased in recent years.[1,2] While content of these programs was related to improving skills and imparting new knowledge, they were seldom evaluated in terms of actual improvement in the performance of participants.

Accurate and precise laboratory results are required by physicians for good medical care. Surveys show that laboratories in small rural hospitals are more likely to produce inaccurate results.[3-7] The personnel in such hospitals are also less likely to have access to educational programs which can aid in upgrading their skills.[4]

In June, 1970 the Minnesota Society of Medical Technologists initiated a project in continuing education which was designed to upgrade laboratory performance in 125 small rural hospitals. The project, Continuing Education for Laboratory Personnel (CELP Project), was conducted over a period of 21 months. In order to bring continuing education close to the work location, two familiar types of programs were offered: (1) regional workshops and (2) consultation visits. Content of both programs was geared to the basic skills and functions of personnel in small hospital laboratories.

The project design was developed to provide an objective means of evaluating the effectiveness of the programs on improving laboratory performance. Workshops and consultation were offered alone and in combination so that the relative effect of each type of program and the possible reinforcement effect of combining them could be studied.

This demonstration project was sponsored by the Minnesota Society of Medical Technologists. It was a component of Northlands Regional Medical Program, Inc. supported by HEW grant #5 GO3 RM-00021. The opinions presented do not constitute endorsement by NRMP, Inc. or the Department of Health, Education and Welfare.

Methods

During the initial planning phase, the 125 individual hospitals were divided into three groups —workshop, consultation, and combined workshop and consultation. Personnel from hospitals in the workshop group were invited to regional workshops. Personnel from hospitals in the consultation group were scheduled to receive individual consultation visits. The personnel in the combined group hospitals received invitations to the workshops plus individual consultation visits.

The 1970 Directory of Licensed Hospitals and Related Institutions was used to identify small rural hospitals and their locations. Small hospitals were defined as those with a capacity of less than 100 beds.[5,8] Rural hospitals were defined as those lying outside the metropolitan areas of Minneapolis-St. Paul and Duluth. The state was divided into eight regions having fairly uniform distribution of small rural hospitals (see Figure).

Educational background of the laboratory personnel was identified by means of a Minnesota Department of Health questionnaire. Personnel were placed in two categories according to their educational background: "specialist/technologist" and "lab technician/aid." The "specialist/technologist" is equivalent to a registered medical technologist with four years of educational background and certified MT(ASCP) by the American Society of Clinical Pathologists. The "lab technician/aid" includes ASCP Certified Laboratory Assistants (CLA), Minnesota certified Medical Laboratory Assistants (MLA), proprietary school graduates, military trained technicians, and on-the-job

trained technicians. All personnel in this category were considered to have educational backgrounds equivalent to one year of formal training.

Hospitals were then classified according to the educational background of their laboratory personnel into two classes:

Class I—those employing at least one four-year person ("specialist/technologist")

Class II—those employing only one-year people ("lab technician/aids")

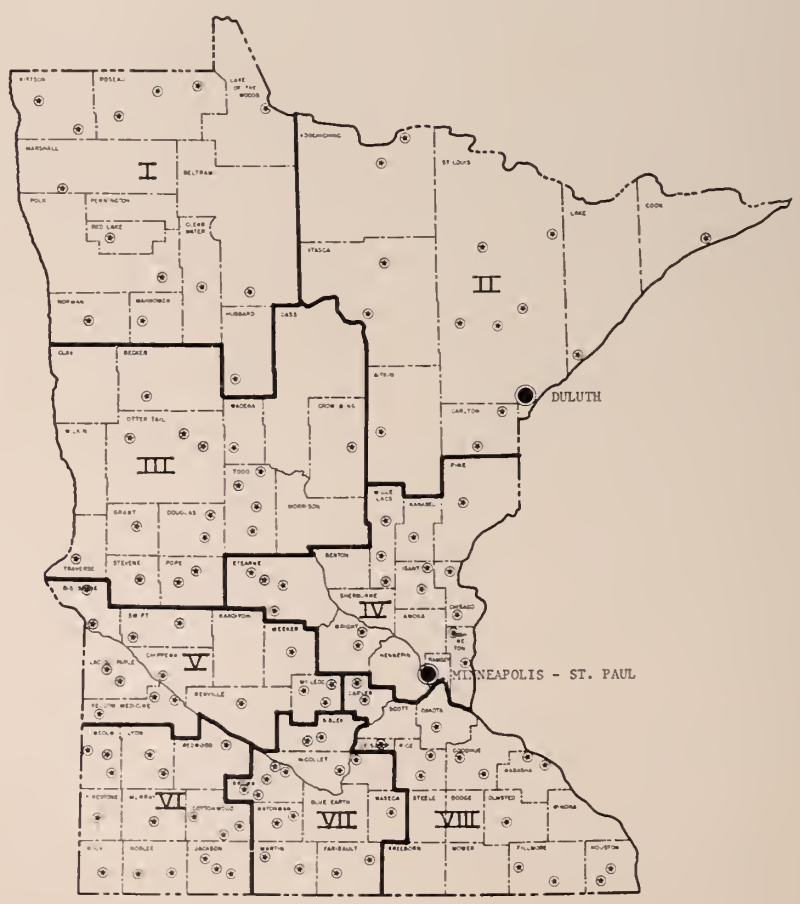
Once classified, hospitals were randomly assigned by class within each region, to one of the three educational program groups. Table 1 shows the distribution of hospitals in each group among the eight regions.

Two letters were sent to each hospital administrator announcing the project and requesting his cooperation, first by the Project Director and second by the executive director of the Minnesota Hospital Association. Although initial response was good, followup communication was necessary to achieve maximum participation.

Workshop Programs

Area vocational technical schools with MLA programs, junior colleges, state colleges, and branches of the University of Minnesota were selected as workshop sites in the eight regions. Site visits were conducted to determine adequacy of equipment and facilities and to gain the cooperation of school administrators. Scheduling of regional workshops began in October, 1970 and continued through December, 1971.

Two series of workshop programs were developed and presented. The format included lecture demonstrations and slide presentations as well as laboratory exercises. Program content covered the four major laboratory subjects—blood banking, clinical chemistry, hematology, and microbiology. The information on educational background of personnel showed that there were 2.7 times as many one-year technicians employed in the hospitals as four-year technologists. A mixed audience with regard to background and experi-



Figure

TABLE 1
Assignment of Hospitals to Groups
According to Class and Region

Region	Number and Class of Hospitals in Each Comparison Group						
	Consultation		Combined Consultation and Workshop		Workshop		Total
	Class I	Class II	Class I	Class II	Class I	Class II	
Region I	2	3	1	3	1	4	14
Region II	2	3	2	3	1	3	14
Region III	1	4	2	4	2	4	17
Region IV	3	3	3	2	3	3	17
Region V	3	2	3	2	2	3	15
Region VI	2	4	2	4	2	3	17
Region VII	2	3	2	3	3	3	16
Region VIII	4	1	4	1	3	2	15
Class Totals	19	23	19	22	17	25	
Group Totals	42		41		42		125

*Class I—hospitals employing at least one four-year person.
Class II—hospitals employing only one-year people.

ence was anticipated, and content was therefore geared to a basic level. Open discussion was encouraged to provide a forum for more advanced questions and specific problems.

Both series of two-day workshops consisted of half-day or full-day sessions in each of the four subjects. The workshops were scheduled on a Friday and Saturday in each region to facilitate attendance for those individuals who could not leave work easily.

Consultation Program

Consultation was carried out by staff technologists in the same four subject areas emphasized in the workshops. Visits were scheduled with consent of the hospital administrator and laboratory personnel. Consultation was also conducted by telephone and request visits were scheduled as needed. Scheduling of visits began in October, 1970 and continued through March, 1972.

Equipment and routine procedures were inventoried during the first visit. Correspondence and reports of each visit were kept to maintain up-to-date information on recommendations and changes in procedures which were adopted. The laboratory's most recent report from the Clinical Chemistry Study[9] was used to determine consultation needs for specific chemical procedures. As consultation progressed, a collection of new procedures and revisions in technique were developed. These procedures and techniques were then offered to laboratory personnel during subsequent visits for information and implementation.

Methods of Evaluation

Separate questionnaires were developed by the workshop faculty for each workshop. Participants were asked to complete a questionnaire for each session stating his feelings regarding relevance of the topics to working situations, level of subject content, pacing of the presentation, and future topics of interest. An information form was also used to poll preference of days for future workshops.

Responses to questions on pacing obtained after the first workshop in each series were used by the faculty to judge and correct the speed of presentation in subsequent presentations. A poll of the requests for future topics was used to determine subject matter for the second series of workshops.

The effectiveness of consultation was based on the personal observations of the staff technologists during and following the visits. These observations were recorded in the consultation reports for future reference.

The objective evaluation consisted of measuring the effectiveness of the two educational programs, offered alone and in combination, on improvement of laboratory performance in chemistry. Performance was evaluated by using the results generated by those laboratories participating in the Clinical Chemistry Study, a voluntary proficiency program of the Minnesota Department of Health.[9] This evaluation is currently being carried out by comparing laboratory performance before the project started and after the programs were completed. The details of the design and results will be published elsewhere.

Results

Minnesota has a large number of small hospitals —134 of the 184 licensed general hospitals, or 73%, have capacities of less than 100 beds. Nine of these are located in metropolitan areas where resident pathology services and ASCP registered medical technologists are readily available. The remaining 125 are distributed fairly uniformly across the state with less density in the upper third where lakes and forest lands predominate (see Figure).

The response of hospital administrators and laboratory personnel to our invitation to participate in the educational programs was especially gratifying. Of the 125 hospitals, 123 agreed to participate (99%). One hospital closed shortly after the programs started, and one hospital refused to participate.

Participation in Workshops

Actual participation of the laboratory personnel in the workshops is shown for both the workshop and combined groups in Table 2. The workshop group maintained a level of 60% participation during both series of workshops. Although all but one hospital had agreed to participate, 11 never actually sent personnel to any workshops. The other 29 hospitals were represented at one or both of the series, and 24 hospitals were represented at each series. The reasons for nonparticipation seemed to be personal; there was no difference in size or geographic location between those hospitals represented and those not represented.

The combined group showed slightly less participation than the workshop group (45-55% compared with 60%). Fifteen of the hospitals in this group never sent personnel to any workshops. Again there was no difference in size or geographic location between hospitals represented and those not represented. All of these hospitals received consultation visits as part of the combined group program. Perhaps some of them felt that the personal consultation method was adequate for their needs.

Although participation was less in the combined group, the difference was small. This demonstrated the popularity of the workshop programs. The total participation figures for the 82 hospitals invited to the workshops was 57% for the first series and 52% for the second. Eliminating the 11 hospitals in the workshop group which were never represented, and therefore did not participate in any aspect of the project, there was an overall level of 90% participation in the project among the 124 hospitals.

Participation in Consultation

Two or three visits were made to each laboratory receiving consultations during the 18 month period—a total of 203 visits. Because the staff technologists traveled to them for consultation services, the personnel in the consultation and combined groups were a captive audience and participation was therefore 100%. Effective consultation during the initial visits was delayed until personal rapport could be developed between the personnel in the laboratory and the consulting medical technologist. Laboratory personnel were encouraged to telephone collect if they had problems between visits. This service was not used extensively, but the frequency of calls increased during the latter months of the project. Towards the end of the project laboratory personnel began to take full advantage of all consultation services.

Evaluation and Comparison of the Two Educational Methods

The opinions expressed by participants on the workshop evaluation questionnaires showed that the content level was appropriate (Table 3). Re-

TABLE 2
Participation in Workshops

		First Series			Second Series			
	Number of Hospitals in Group	Hospitals Represented	% Participation	Persons Attending	Hospitals Represented	% Participation	Persons Attending	Number of Hospitals Never Represented
Workshop Group	40	24	60%	49	24	60%	49	11
Combined Group	42	23	55%	44	19	45%	39	15
Total	82	47	57%	93	43	52%	88	26

TABLE 3
Participant Response to
Questions Concerning Workshop Content

First Series	Number Responding	Relevant to Work	Plan to Apply*	Satisfactory	As Anticipated*	Too Advanced	Too Simple*
Blood Grouping Problems	45	84%	....	84%		7%	0
Quality Control, Instrument Calibration & Troubleshooting	53	100%	....	96%	....	2%	2%
Red Cell Morphology	47	98%	98%	77%	38%	0	
Common Pathogen Identification	52	98%	....	83%	....	10%	2%
Second Series							
Crossmatching Problems	62	100%		96%		2%	0
Colorimetric and UV Enzyme Determinations	48	90%	....	100%	....	0	0
White Cell Morphology	60	100%	97%	75%	48%	0	....

*Blank indicates question was not asked.

sponses to content of Red and White Blood Cell Morphology workshops show lower percentages than the others. This is due to the fact that participants were given the opportunity to give one or both of two answers—"satisfactory" or "what you anticipated."

On the whole, the faculty felt that the workshops were very successful in terms of satisfying needs of the learners in the subject areas presented. Feedback from individuals during discussion periods and requests for duplicate sets of some of the materials used, indicated that many of the participants intended to share the information with others in their laboratories who were unable to attend.

Consultation was more difficult to evaluate because of the individualized approach used. Personal rapport increased as the consulting staff technologists made repeated visits. Rapport with some of the personnel in the combined group was reinforced by attendance at the workshops. This relationship increased opportunities to suggest changes and recommend new or different procedures. In a few instances, the laboratories were so well staffed and current in their procedures that the consultation visits were little more than social calls. In most cases, however, a great deal of new or additional information was supplied, and laboratory personnel were very interested in expanding their background knowledge and applying the new knowledge to their working situation.

The reinforcement obtained by combining the two educational methods seemed to have the greatest effect on upgrading laboratory performance. Workshops provided a classroom group approach to presenting general information, while consultation afforded personnel in individual hospital laboratories the opportunity to obtain specific information for their needs. Whether the combined methods actually produced the most improvement in performance will be determined by the statistical evaluation currently being conducted.

Other studies have shown that participation in proficiency or evaluation programs has resulted in improved performance.[7] Of the 123 hospitals participating in the project, 87 had been participating in the Clinical Chemistry Study for one to three years. Improvement in performance resulting from participating in that proficiency program should have taken place before this project began. Therefore, if additional improvement in performance is documented, it can be directly attributed to the educational programs offered.

Discussion

Since the regional workshops were conducted on an invitational basis, participation was voluntary. Two factors had a considerable effect on attendance—weather and vacations. Blizzard conditions during the first series of workshops caused rescheduling twice in one region, and the travelling faculty was trapped both times. Attendance also dropped off during the summer vacation months. Small hospitals have greater difficulty than larger hospitals in providing coverage during vacation periods. Spring and fall proved to be the best times of the year to conduct regional workshops in Minnesota.

Although the workshop participation was less than we had hoped for, the overall level was greater than that experienced in an earlier study in Minnesota dealing with evaluation of blood bank training programs.[6] In that study continuous training courses were required of personnel in 39 hospitals, and central and regional training courses were made available to the remaining 115 hospitals participating in the study. Only 36% of the

115 hospitals were represented at the central and regional training courses. Since the students attending the courses varied widely in basic education and experience, instructors found it difficult to set the level of instruction to meet all student needs. Students with brief basic education were reluctant to ask questions when they didn't understand, and reluctance increased when more fully trained students were present.

We experienced similar reluctance to ask questions among some of the participants at our workshops. However, concerted efforts of the faculty to keep the content basic, to elicit response during the discussion periods, and to maintain a casual, friendly approach resulted in adequate to lively response from most of the participants. Individuals who were reluctant to speak out in the group frequently asked questions on a personal basis during coffee breaks and lunch.

The need for and benefit derived from continuing education programs for laboratory personnel in small hospitals has been noted by Sattler in her report of a similar RMP sponsored program in Washington and Alaska.[10] That program differed from ours in that travel expenses were provided to bring people into centrally located laboratory training centers for refresher and on-the-job training, rather than to carry the programs out to the area of employment. The training sessions were not formal sessions, but were individualized instruction sessions applicable to the person's own laboratory situation. After three years of operation, 74% of their 156 trainees had come from hospitals of 100 beds or less.[11]

Although cost figures are not readily available, the CELP Project and the Washington/Alaska continuing education program are expensive programs to carry out. It is not known at the present time which of these approaches is most efficient economically or most effective in actually upgrading performance. The question of determination of economic efficiency would require development of new techniques for cost accounting analysis. Continuing education programs have rarely been evaluated in the past in terms of actually producing improvement in performance. Hopefully, the objective evaluation studies of both of these programs will answer the question of effectiveness in improving performance.

Summary

During the past two years, the Minnesota Society of Medical Technologists has conducted a program in continuing education for laboratory personnel in small rural hospitals. Program activities included regional workshops and consultation visits to individual hospital laboratories. Four laboratory subject areas were covered—blood banking, clinical chemistry, hematology, and microbiology.

The 125 small rural hospitals were divided into three groups—consultation, workshop, and combined consultation and workshop. Out of the 123 which agreed to participate, 112 hospitals participated in one or more of the educational programs offered.

Over an 18 month period, 56 regional workshop programs were presented and 203 consultation visits were made. Once personal rapport was established, the consultation visits became quite effective. Participation in the workshops exceeded 50%, and response from participants was highly favorable for content and application.

Although objective data on improvement in performance has not yet been analyzed, the technique of combining regional workshops and personal consultation visits seemed to be better than providing either program alone.

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